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HYPOPARATHYREOSIS, STATUS PARATHYREOPRIVUS, AND TRANSPLANTATION OF THE PARATHYROID GLANDS.

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We have no term except tetany to express the condition resulting from an insufficience of parathyroid tissue or parathyroid secretion. Probably the explanation of this is the fact that hitherto no instance of what might be termed hypoparathyreosis of a degree less than the tetanic one has been described. I would, therefore, propose Status Parathyreoprivus and Hypoparathyreosis as appellations to designate the state of the individual suffering from partial or complete loss of parathyroid tissue.

We have had the exceptional opportunity to observe for about fourteen months symptoms due to parathyroid extirpation or destruction and ameliorated at times by the administration of the parathyroids of beeves. Tetany has not been permitted to develop nor the manifestations of deprivation of parathyroid secretion to mature sufficiently for the production of the Trousseau or the Chvostek phenomena. We might define the condition of this patient as subtetanic hypoparathyreosis.

The first to describe in recognizable form the affection which we term tetany was a German named Steinheim, who in 1830 termed it Hitziger Gelenkrheumatismus, believing that the disease was closely allied to acute multiple articular rheumatism. The following year there appeared a publication by Dance entitled *Observation sur une espèce de tetanos intermittent.* This author recognized the

essential feature of the affection, the intermittent character of the attacks of spasm.

Within the next few years numerous articles by French authors were published on contractures of the extremities, which, however, shed very little light on the subject. The especial contributions to the knowledge of this disease rendered by Trousseau, Erb, Chvostek, and other more recent writers are probably well known. In 1845, Trousseau, having observed the attacks in a nursing woman, termed the affection "contracture rhumatismale des nourrices." But in 1852 the disease was carefully studied by Lucien Corvisart, who proposed for it the name tetany, an appellation which it has since maintained.

Tetany has been observed as an endemic, an epidemic, and a so-called idiopathic form in apprentices of various forms of hand labor; in infections, including malaria; in intoxications; in gastro-intestinal disturbances; after exposure, particularly in children; during teething; in Bright's disease; in pregnant, confined, and nursing women; as a symptom in certain affections of the nervous system; after operations for goitre.

In 52 extirpations of the thyroid gland in Billroth's clinic, tetany occurred 12 times, or in 23 per cent. of the cases; death occurred in 9 of these. Von Eiselsberg in 1890 stated that 30 cases of tetany due to thyroid extirpation had been observed. Of these, 7 are said to have recovered, 3 to have suffered chronically from the affection, and 13 to have died. The result in the remaining 7 cases was unknown. Of the 12 carefully observed cases of Billroth there was, probably, 1 recovery; 2 cases became chronic. A number of chronic cases of operative tetany have been observed, some of them for many years, by various surgeons; these patients are reported as having periodic attacks of tetany at irregular intervals, and as being quite well between these tetanic manifestations. Total extirpation of the thyroid yielded a much greater percentage of tetany in the hands of some operators than of others; and so before anything was known of the parathyroid glands total extirpations were rarely undertaken except for malignant disease. In several of these cases fatal tetany occurred.

The study of our case of aborted operative tetany has been greatly facilitated by the coöperation of the unusually intelligent patient, a cultivated woman who, prior to the operation, was in excellent health except for the distress of a large and rapidly growing goitre. On May 5, 1904, I excised, for this patient, at the Johns Hopkins Hospital, the left lobe of the thyroid, endeavoring to leave *in situ* both of the parathyroids of this side if possible. A careful examination of the removed lobe, by Dr. MacCallum as well as by myself, did not reveal a parathyroid gland. The patient returned March 26, 1906, to be relieved of the asphyxia and apprehension caused by the remaining lobe, which from the usual change in position following

the unilateral operation, and from a very considerable increase in size, resembled, on superficial examination, a bilateral and rather symmetrical, large goitre. The patient having said to me before operation, "Remove it all if you can, for I would rather take thyroid extract the remainder of my life than have the goitre return," and as the goitre had grown rapidly since the previous operation I determined to remove as much of the thyroid proper as could, in our opinion, safely be done. Although the goitrous lobe was carved in a way which I thought would not endanger the lower parathyroid gland, the knife actually grazed the edge of this body, which I detected immediately on the excised portion of the right lobe, in quite a normal relation to a branch of the inferior thyroid artery. It happened that on the preceding day I had performed the same operation, and in much the same way, for a goitre of the right lobe of the same kind, on a patient whose left lobe I had removed seven years ago. A stump of the same shape and in the same position was left, but it contained, presumably, the right inferior parathyroid. In both patients the four thyroid arteries had been tied in the course of the two operations on each. We watched the convalescence of the patients carefully; the one first operated upon recovered without incident, but the second was not herself from the outset, although her temperature and pulse were about normal. "This recovery is entirely different from the previous one," she would frequently remark. "I do not understand myself. I have never felt so before." She was unnaturally flushed for two or three days; was restless and slept badly. But she believed herself to be improving until the seventh day, when queer feelings developed, so emphasized at times that she designated them as attacks, although she was uncomfortable and a little apprehensive between the attacks even at this time. It is interesting to note that even in the beginning, when the symptoms were very indefinite and mild, they became concentrated in a way to suggest periodic explosions.

My daily visit to the patient was omitted on the seventh day. On the following day, the eighth since the operation, she had, during the morning, several "attacks," and at my visit, about 2 P.M., I found her quite excited and not a little apprehensive. While attempting to describe her feelings in these attacks or "spells," there developed one, superinduced, it seemed, by the incidental increase in mental activity. It passed through phases precisely as she had described them for the previous attacks. "I feel a numbness in my lips as if the blood had stopped in them; a sort of wave of numbness is passing over my face;" and a few seconds later, "Now it is going into my arms; now it is passing off. Oh, it is dreadful! I would really rather die than have even a few more attacks like these. They are indescribably awful." On the disappearance of the "numbness" or lifeless feeling of the lips, for example, it seemed to the patient as if the blood which had suddenly been blocked

was rapidly let into the affected parts again. We were unable to see variations in the appearance of the lips during the attack. The patient insisted that she could not have closed her eyelid without a finger if her life had depended upon it. This suggests hysteria, but those who saw her in this attack doubted not the existence of a very serious condition. She looked ill, quite alarmingly so. Dr. MacCallum, appealed to in haste, placed at our disposal his entire collection of the dried parathyroids of beeves. I was so concerned about the patient and so confident as to the nature of the symptoms that it did not occur to me to make the Chvostek and Trousseau tests until several parathyroids had been given, and even then I feared for several days to make prolonged pressure on the femoral artery, or to test the electrical reactions. The effect of parathyroid exhibition was almost instantaneous and most marvellous. Large doses were given at first, six dried glands every three hours.

Hoping to stimulate hypertrophy of any parathyroid tissue which might still be in the body we reduced the number, in the course of a few days, gradually to one gland three times daily.

The patient could not, for several weeks, bear further reduction in the dose of parathyroids, although she was perfectly willing and almost eager to attempt it, notwithstanding her feeble and strange, neurasthenic-like condition.

Tapping the facial nerve, repeatedly tried, has not once elicited a response. Nor has pressure of the femoral artery, exercised for periods of four and five minutes, been followed by contractions.

Naturally of a most cheerful and optimistic disposition, she made a brave fight during brief frequent, dispiriting periods, of which the duration was rarely more than a few hours—often only one, though occasionally twelve. Attempts to test electrical reactions distressed her so acutely that they were given up. Convergence tests of the internal recti muscles unnerved her; she involuntarily frowned when the finger approached the nose, as if the effort to follow it were actually painful. A slight, hard œdema of the legs between the knee and ankle and a cold skin persisted for weeks. For a brief period there was albumin in the urine. Sudden changes of weather, particularly to cold, affected her badly. On showery days she would say, "I feel precisely as if I were taking electricity." She expressed at the outset great aversion to sweets and a desire for acids, but when parathyroids had been given for perhaps two days she nibbled bonbons with relish.

For the eight days after operation and preceding the administration of the beeves' parathyroids there was a rapid loss of weight. After the administration of parathyroids was instituted there was for several months a slow gain in weight.

Our patient remained in the hospital for twelve (?) weeks after the operation, taking the fresh parathyroids of beeves at times in large amounts during the entire period, except for the first thirty-six

hours after the development of the privation symptoms and on the few occasions when the dried glands were substituted for the fresh, either for the sake of comparison or because the supply of fresh parathyroids had been unexpectedly interrupted. Their exhibition was by mouth only, as prolonged hypodermic administration of the crushed glands could not, it seemed to us, be endured, owing to the physical properties of the emulsion, the bulkiness of the dose, and the annoyance and danger from the hardly avoidable infection. The patient promptly discovered, as did we, that the dried glands, a nauseous dose, seemed less effective than the fresh.

In preparation for ingestion the fresh glands were carefully freed from fat, chopped very fine, and served on thin, crisp water-crackers. The dried, powdered glands were usually given in gelatin capsules. During the summer and autumn of 1906 the patient, at home in the South, took the dried glands. Their discontinuance in November, 1906, for about three months was without effect, appreciable either by the patient or her family; and after resumption of the parathyroid feeding for about one month without benefit the ingestion of the dried preparation became so revolting that its exhibition was discontinued.

March, 1907. From correspondence I judge that the patient has in some ways slowly improved. There has been a little gain in appetite and in strength, and, as I have said, a considerable gain in weight. But she is an invalid. Her nervous system is quite wrecked. Conversation, even of a light and bright nature, unnerves her; so does a walk of one hundred or fifty or a less number of yards, or even sitting up in a chair for an hour or two. Shall we term this condition a cachexia parathyreopriva? And may not, in some cases, the cachexia thyreopriva, so called, be compounded of thyroid and parathyroid privation? Cachexia thyreopriva must be studied from a new point of view. Our patient writes that during the past three or four months pain in her knees, elbows, and shoulders is quite constant and at times distressing. There is, perhaps, no pain except that induced by motion, although this may persist for many minutes, particularly after some hasty, uncalculated movement. Exercise of the knees elicits crackling noises which at times may be heard by those at the bedside. The nature of this affection of the joints, or joints and tendons, has not been determined.

I have it in mind to make hypodermic injections of the parathyroid-nucleoproteid which Dr. Beebe, of New York, is now, he kindly tells me, experimenting with, and hope that the experiments in transplantation of the parathyroids in animals which I have been conducting since January may give results to encourage the therapeutic use of this measure in the case of our patient for whose pitiable plight I am responsible.

Picture the operator's state of mind if, instead of one, a number of cases of tetany or hypoparathyreosis were placed to his—shall I say,

credit? A certain measure of consolation is found in the knowledge that the deplorable result was brought about in the effort, fortunately successful, to cure a hardly endurable condition, one which menaced life. The patient charitably insists that her present state is preferable to the wholly intolerable one from which the operation freed her.

THE TRANSPLANTATION OF PARATHYROID GLANDS. I had been seriously deliberating as to the advisability of attempting subperitoneal transplantation of the parathyroids for this patient when there appeared the impressive report of Payr[1] on the successful transplantation of portions of the thyroid gland into the spleen, both in animals and the human being. From Payr's concluding summary I abstract the following: The spleen possesses, thanks to its altogether peculiar and rich blood supply, unusually excellent conditions for the transplantation of all kinds of tissue. The circulation is rapidly restored, a relatively small proportion of the transplanted part is sacrificed to central necrosis, and the processes of regeneration are more active and more extensive than in any of the methods of transplantation heretofore employed. The chief consideration against the transplantation into the spleen is the danger of hemorrhage. But by numerous experiments in animals a technique has been developed which has effectually overcome this danger. Chief among the technical features are the use of the transplanted organ as a wedge in the splenic wound and of the omentum as a support for the stitches and a covering for the line of incision in the spleen. It has been possible by this method of splenic transplantation to keep alive for a period as long as three hundred days animals which otherwise would have perished with symptoms of insufficience of the thyroid gland. Into the spleen of a child, six years old, totally imbecile and with severe infantile myxœdema (treated almost without result for a period of three and a half years with thyroid feeding), a large piece of the thyroid gland of the perfectly healthy mother was transplanted. The result, to the present time, somatically as well as intellectually, is highly satisfactory.

Payr's work stimulated me to attempt splenic transplantations of the parathyroids on dogs with the hope that if successful I might do the same thing for my patient. As the result of a very considerable experience in thyroid transplantation gained by me in 1888 the spleen seemed an ideal organ for the purpose. The technique of the thyroid transplantation as developed by Payr was very simple. The block of thyroid tissue used as a wedge assisted in the arrest of hemorrhage from the spleen. But the tiny shavings of disks of parathyroid tissue could not play such a role, and at first I found the bleeding from the little holes made bluntly in the spleen annoying because it prevented

[1] Transplantation der Schilddrüsengewebe in die Milz; experimentelle und klinische Beiträge, Langenbeck's Archiv, Band lxxx, p. 730; also Verhandlungen der Deutsche Gesellschaft für Chirurgie, 35te Congress, I, 155, and ii, 503.

the introduction of the parathyroid films, promptly floating them entangled in a clot to the surface. After a few unsuccessful trials the following procedure was devised: A split thread of china-bead silk is armed with two very fine needles, No. 16. The properly prepared parathyroid, or preferably the little supporting rim of thyroid gland, is perforated with one of the needles and the minute gland slipped an inch or two on to the thread, great care being exercised to avoid crushing it. A little hole is made in the spleen with a fine-pointed artery forceps, the blades of which are opened wide enough to admit the parathyroid between them. Both needles, first one and then the other, introduced between the blades of the artery forceps down to the apex or bottom of the hole made in the spleen, transfix the spleen and emerge on the opposite side a few millimeters apart. The thread ends are pulled upon until the transplanted piece is carried to the bottom of the hole prepared for it. The spleen is then darned very gently with a mattress stitch or two of this split china-bead silk on the fine needles carried from quite a distance on both sides across the base and middle of the hole, and finally one of the threads which have been held taut is divided close to the under surface of the spleen and withdrawn. This method serves infallibly to fix these tiny films in the desired position. The bleeding from extensive tears, crushings, or cuts may be controlled by this method of darning.

As the threading of these very fine needles is difficult, the double arming of the silk may be avoided by a slight modification of the procedure, which we have used of late. A single needle, threaded, is passed from the under surface of the spleen upward into the apex of the transplantation hole, made in the manner described; then, impaling a parathyroid, it is carried back into the hole from which it has just emerged and thence through to the under surface of the spleen a few millimeters from its point of entrance.

In the dog the inferior parathyroids in preference to the superior have been selected by me for transplantation, because being partly embedded in the thyroid gland and thus splinted by it they may be shaved with a sharp cataract knife or fine scalpel, on the exposed surface. Under and about the parathyroid a little thyroid tissue should be left. Thus framed in thyroid tissue the tiny parathyroid disk can conveniently be manipulated and speared by the needle without injury.

The thyroid glands, particularly when hypertrophied, as in Graves' disease, should serve admirably for transplantation of the parathyroids. On several occasions, operating for exophthalmic goitre, I have transplanted back into the other lobe or into the isthmus a parathyroid whose nutrition was cut off or imperiled. Once the parathyroid so transplanted had been unintentionally excised. In a case of carcinoma of the stomach with gastric tetany and in the course of an operation for gastro-enterostomy, I attempted transplantation into the spleen of fresh parathyroids, obtained by Dr. MacCallum and Dr. Sowers from a body dead only about an hour. Unfortu-

nately at the instrument table a drop or two of a solution of carbolic acid accidentally came in contact with these parathyroids, and hence I desisted from the attempt to transplant them, although the spleen was in my hand and already prepared for the transplantation.

I had the pleasure of demonstrating a few months ago at my clinic, and before the Interurban Clinical Club, which complimented me by attending it, microscopic sections showing the morphologically successful transplantation in dogs of parathyroids into the thyroid gland, and I hope to be able to report soon the result of functional tests.

We have transplanted parathyroids into the thyroid gland and spleen in 17 dogs. On each of two occasions as many as 8 dogs were used in the search for a large number of suitable parathyroids for splenic transplantation. In the spleen of each of 3 dogs as many as 7 parathyroids were at one time transplanted.

Tetany, inexplicable so recently as eighteen years ago, has been made comprehensible by one of the greatest and most impressive physiological discoveries of modern times. Four or more tiny bodies, so small as to have attracted no serious attention until, in 1880, Sandstrom classified them, quickly assumed upon the epoch-making discovery of Gley, in 1891, an importance hardly to be overestimated. Their situation, so deep in the neck, so carefully tucked away under the jaw and behind the thyroid lobes; their nutrition, each gland with a blood supply independent of the other and in no danger of cut off except by the surgeon's knife; and their number, generally four or more, might be viewed to indicate their preciousness. Their blood supply is a rich one and may well be subject on occasion to great and sudden increase, as in the active thyroid hypertrophies and hyperemias. Their vascular supply is so intimately related to and dependent upon that of the thyroid that they could hardly escape, it would seem, promptly and altogether, the effect of a sudden turgescence of the thyroid lobes, although controlled undoubtedly by regulating vital processes. The possibility of an interdependence of function between the thyroid and parathyroid glands has suggested itself to several investigators.

In this connection the "Note during Proofreading," appended to Dr. Reid Hunt's article on "The Influence of Thyroid Feeding upon Poisoning by Acetonitrile," is very interesting: "Later experiments show that feeding with parathyroids does not decrease the susceptibility of mice to acetonitrile; on the contrary, it causes a distinct increase of the susceptibility to this poison. Whether this increase of susceptibility is greater than that caused by an equivalent amount of proteid has not been definitely determined, but the indications are to this effect."

In Lusena's hands after experimental parathyroidectomy the average duration of life was only half as long as after parathyroidectomy plus thyroidectomy.

In this connnection certain experiments on dogs made in 1888, and before we knew that the parathyroids had any function whatever, may be in point; in the light of our present knowledge they furnish interesting material for speculation. In a few instances[2] I

[2] W. S. Halsted, An Experimental Study of the Thyroid Gland of Dogs, with Especial Consideration of Hypertrophy of this Gland, Johns Hopkins Hospital Reports, vol. i, Baltimore, 1896, p. 378.

Partial Isolation of Both Thyroid Lobes. The large branch of the thyroid artery which goes to the upper pole and the vein from the lower pole are not ligated; otherwise both thyroid lobes are completely isolated.

Example 1. Dog 104.

April 19, 1889. Open wound.

April 28. The dog seems perfectly well. The wound is healed.

April 30. The dog has tongue tremors and makes the licking movements with the tongue which we have frequently observed in dogs whose thyroids have been extirpated.

May 1. The tongue tremors are less pronounced. The licking movements are still vigorous.

May 7. The tongue tremors are pronounced. The dog has no general spasms.

May 14. The tongue tremors are very faint.

May 28. Dog seems perfectly well.

June 24. Hair is falling out, particularly over the eyes.

June 25. The dog has escaped.

June 27. Returned of his own accord. The hair is very thin all over his body. He scratches himself constantly. The œdema caused by the scratching gives to the skin about the face and head somewhat the appearance of myxœdema.

July 10. Has lost most of his hair. He is very anemic. His blood is used for direct transfusion into dog 109.

Autopsy. Both thyroid lobes are large and hard and very firmly bound down to the surrounding tissues by adhesions. With the microscope they were found to be hypertrophied. I believe, judging from the next example (dog 103), that this dog would have died ultimately with the symptoms of thyroid extirpation.

Example 2. Dog 103.

April 19, 1889. The wound is left open. The dog was profoundly depressed after the operation.

April 27. There is conjunctivitis of both eyes. The wound is doing well.

April 28. The dog has symptoms which are characteristic of extirpation of both thyroid lobes. He shivers, has tongue tremors, and general tonicoclonic spasms. His gums are inflamed. The membranæ nictitantes are conspicuous. He groans with each expiration.

April 30. The tongue tremors persist. The general spasms have ceased. The conjunctivitis is more pronounced. There is a very offensive gingivitis. Dog makes peculiar, almost incessant licking movements with his tongue. These peculiar licking movements have been frequently observed by me in dogs whose thyroid glands have been extirpated.

May 1. Seems better. He still has tongue tremors.

May 3. His hind legs are slightly stiff. The tongue tremors are scarcely perceptible.

May 7. The tongue tremors are more distinct. The conjunctivitis has almost subsided.

May 14. The tongue tremors are very faint. There is no conjunctivitis.

May 19. All the symptoms of extirpation of both thyroid lobes have reappeared.

May 21. The dog seems much better. The tongue tremors are very faint. There are no other symptoms. There is a slight subconjunctival injection.

May 23. Except for the faint tongue tremors the dog seems fairly well. He eats well, but is very thin.

May 24. Has no tongue tremors, but strong clonic spasms of the flexor muscles of all of his legs. The spasms of the temporal and ear muscles are especially pronounced.

May 25. Dog has no spasms and is much better.

June 14. All the symptoms of double extirpation have reappeared.

June 15. A.M. Dog found dead.

Autopsy. The left thyroid weighs 3 gms. and is very hard. The right thyroid weighs 1 gm. For the microscopic appearance of both lobes see Plate X, Fig. 7. The fatal result in this and the preceding case (104) is to be attributed probably to extensive destruction of the glands by blood extravasation. Otherwise we could not regard the changes which we designate as hyper-

ligated all the vessels, veins and arteries of both lobes, except the superior thyroid artery and the inferior thyroid vein. In these cases the dogs ultimately died, notwithstanding the fact that as a result of the operation the thyroid lobes enlarged and microscopically showed the hypertrophic picture. These cases puzzled me greatly in those days, when tetany was believed to represent acute thyroid privation, for a modified and chronic tetany occurred, notwithstanding the hypertrophy of both thyroid lobes. Dogs so treated lived nearly three months on the average, in contrast to those with thyroid extirpation, which died usually in from two to nineteen days after operation. These are perhaps the first recorded cases of chronic experimental tetany. Both superior parathyroids were probably deprived of their circulation by the ligature of the superior vein plus the handling incident to the ligation, but the inferior or subcapsular glands should have had the benefit of a blood supply which was sufficient, not merely to prevent necrosis of the thyroid lobes but to cause their hypertrophy—hypertrophy confirmed microscopically. Hence there should have survived for each dog, it would seem, the two internal parathyroids as well as the hypertrophied thyroids. If the existence of antagonism between thyroids and parathyroids were established we might assume that the hypertrophied thyroids were imperfectly equilibrated by the two parathyroids, and that if thyroid hypertrophy had not resulted the two inferior or subcapsular parathyroids would have been more than ample for the prevention of tetany. This is the merest speculation and indulged in to call attention to the experiments which are, I believe, unique and might some day be repeated. In such case the interest would concentrate in the condition of the inferior parathyroids. With no parathyroid tissue remaining the dogs could not have lived, as they did, for months. The open wound and consequent suppuration in our cases may have partially destroyed the parathyroids. The cicatricial contraction may have been a factor plus the infection.

Of particular interest to the surgeon is that form of tetany caused by operation upon the thyroid gland. When total excision of the thyroid was practised for the cure of ordinary colloid and other goitres surgical tetany was comparatively common; then for nearly twenty-five years little was heard of this form of tetany, but now again it is making its appearance with alarming frequency and especially at the hands of the most experienced operators, those who are convinced of the advisability of removing in Graves' disease as much of the thyroid as can safely be done. The distinguished surgeon who was perhaps the first to warn against total excision of the thyroid gland is now among the first to advise for the cure of exophthalmic

trophy as very highly compensatory; for, notwithstanding the fact that the glands weighed two or three times as much as normal and showed the most advanced stage of hypertrophy, one dog died with symptoms of total extirpation and the other had the symptoms which I have described (dog 104), and would probably have died of thyroid privation.

goitre an excision, almost total, of this organ. Within a year or a little more, and in his latest 50 operations this operator has produced 7 cases of tetany; in none of these was the disease fatal, however; although in none have parathyroids in any form been given.

That operative tetany has of late so frequently resulted after a quarter century's interval of freedom from this complication of thyroid removal, is due to the facts that the operation for exophthalmic goitre is becoming much more frequent; that the proportionate amount of the gland removed in this operation is increasing, and that the loss of parathyroid tissue seems to be less well sustained by patients suffering from Graves' disease than by those afflicted with the hypothyreotic or colloid forms of goitre.

THE OPERATION. The development of the operation for exophthalmic goitre is an interesting story. Hemorrhage from the large, thin-walled veins was quite terrifying to the surgeon in the early days of the operation, and only a few weeks ago I heard a brilliant operator at work on a serious case exclaim: "This is like hunting for big game; instinctively, I look over my shoulder for a tree when I tackle a difficult exophthalmic goitre." The mortality from the toxemia of absorption, of blood and of thyroid secretion, was very high. And now the surgery of exophthalmic goitre centres in the problem of removing the greater portion of the thyroid gland without sacrifice of the parathyroids. I know from correspondence with the surgeons abroad who have especially devoted themselves to thyroid surgery that with them this problem is not solved.

I shall take it for granted that the situation of the parathyroid glands is fairly well understood; but a composite chart based on sixty-seven dissections, which were very kindly made for me by Dr. MacCallum, is of interest. The parathyroid bodies vary greatly in size and not a little in situation. The study of the situation of these little bodies in Dr. MacCallum's dissections and the diagrams based thereon and in the cases operated upon by myself, had given me the impression that much the densest grouping of parathyroids, in the composite diagram, would be about the insertion of the terminal branches of the inferior thyroid vessels, and that in comparatively few instances would these bodies have to be represented above or even as high as the tip of the superior pole of the thyroid. From our study, however, it was found that one is likely to encounter these little bodies, usually two on each side, at any level from the superior to the inferior pole on the postero-internal surface of the gland, but most commonly just internal to the rounded postero-external border and quite regularly near the site of the distribution of the terminal branches of the inferior thyroid artery. If the thyroid gland is lobulated in this situation, as is quite commonly the case, a parathyroid may be concealed in a cleft between the lobules. Not infrequently one of these epithelial bodies is located below the inferior pole of the thyroid gland and occasionally behind the sternum.

May the parathyroids be identified with the naked eye in the course of an operation? Yes, and almost infallibly; but perhaps not from any description that I can give. They are little ovoid, spheroid, lenticular, or very flat bodies, exhibiting much variety both in form and size and even in color. Externally they often resemble fat very closely in consistence as well as in color. On section, however, the fat about the deep cervical vessels and in the neighborhood of the thyroid gland is usually much whiter than the parathyroid, and the latter has a definite but exceedingly fine, almost microscopic, granular appearance. Differentiation from accessory thyroids or detached or partially detached lobulettes of normal thyroid tissue, is rarely difficult, although careful comparison of the suspected bodies with the tissue of the goitre may be necessary to convince one as to their nature. Partially or wholly detached portions of certain yellowish goitres, or adenomas of the thyroid, may bear a troublesome resemblance to the parathyroids. Lymphatic tissue is quite readily differentiated by the expert. Differentiation may be impossible if the parathyroids have been subjected to trauma, ever so slight.

The cause of tetany at the hands of well-versed operators is, I believe, less often removal of the parathyroids than interference with their circulation; and I am inclined to feel that the procedure of stripping the posterior capsule, so beautifully executed by Dr. C. H. Mayo, does not guarantee the safety of the parathyroid bodies. To assist in determining this point the removal of one lobe furnishes really no evidence whatever. It is only from the results of operations on both lobes that we can base an opinion. But who, in order to decide the question, will take the risk of causing tetany? I fear to do an operation, even on one side, except in very ill patients, which does not contemplate the leaving of a slice of the thyroid gland in the region of the ultimate distribution of the inferior thyroid artery. I avoid also ligation of the trunk of the superior artery, for fear of injuring the tiny branch to the superior parathyroid, and hence usually slice through the gland a little below the superior pole.

THE INTERPRETATION OF THE PULSATIONS IN THE JUGULAR VEINS.

By James MacKenzie, M.D.,
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Although the venous pulse has been recognized by clinicians for over two hundred years, the exact significance of its meaning today is not quite clear. It is only since graphic records have been taken of the movements in the veins that definite data have been

obtained from which conclusions could be drawn. It was in 1863 that Bamberger and Marey published tracings of the venous pulse, being followed shortly by Geigel and Friedreich, but these tracings were taken independently of any timing with a standard movement. In 1868 Potain obtained tracings of the venous pulse simultaneously with the carotid artery, and after him numerous other observers, notably, Riegel, Francois-Franck, and Gerhardt investigated this subject. The general conclusion arrived at was that there were two kinds of venous pulse: one called the *normal* or *negative* venous pulse, the other the *pathological* or *positive* venous pulse. Generally speaking, this discrimination has prevailed in the literature of this subject.

In 1893,[1] I drew attention to the fact that the varieties of the venous pulse could not be satisfactorily included in these two simple forms, and that clinicians had entirely failed to appreciate the meaning and significance of the various forms of the venous pulse. The terms employed were utterly misleading: the so-called normal venous pulse was often as abnormal as the pathological venous pulse; the negative venous pulse was often largely composed of positive elements, and the positive venous pulse might often show negative evidence. As I had found that the presence of the auricular wave was a constant phenomenon in the majority of cases, I suggested that the term *auricular venous pulse* should be applied to these forms of pulsation in which the auricle occupied its normal place in the cardiac cycle, although in many cases evidence of the effects of the ventricular systole was present as well. On the other hand, I found that what had hitherto been called the positive venous pulse did not show any evidence of the auricular systole at its normal period in the cardiac cycle, and that the whole of the wave occupied the period of ventricular systole; I, therefore, employed the term *ventricular venous pulse*. Further, the appearance of the ventricular venous pulse implies a profound change in the rhythm of the heart, inasmuch as it is the evidence that the heart's contraction starts no longer at the mouth of the great veins.

Variability in the Appearance of the Venous Pulse. To a great extent we are even at this day quite at a loss to explain all the conditions that give rise to a venous pulse. Some people in apparent good health show it, while in cases of marked heart failure it is entirely absent. Some people when in robust health show no signs of it, but if they become slightly debilitated the venous pulse may appear in the neck. In some cases of pernicious anemia the venous pulse may be a very prominent symptom, in others it may never appear. Some women during pregnancy develop a large venous pulse, others develop it only during the puerperium, while others never show the slightest sign of it. In irregular action of the

[1] The Venous and Liver Pulses, etc., Jour. Path. and Bact., 1894, ii. In this article a full bibliography is given up to 1893.

heart it may assume, in certain cases, enormous proportions; in other cases there is not the slightest sign. A man may show it during one attack of heart failure, and during another and more grievous attack may show no sign of it. When one considers the foregoing variabilities in the appearance of the jugular pulse one is compelled to inquire more closely into the mechanism by which it is produced, and it will be found that our knowledge of the heart's action is even at the present day too slight to enable us to speak with certainty.

CARDIAC FACTORS CONCERNED IN THE PRODUCTION OF THE VENOUS PULSE. In order to appreciate fully all the factors concerned it is necessary that we should recognize the very valuable discoveries of Gaskell on the functions, and some observations of Keith on the structure, of the heart. Keith[2] has shown that the musculature of the heart is built up of bands of muscle fibers, having as distinct places of origin and insertion as skeletal muscles, and that each bundle has its function as peculiar to itself as a skeletal muscle. But the heart-muscle fibers are distinct from skeletal muscle in this respect, that according to their special duties certain portions have individual functions more developed than other portions.

The work of Gaskell[3] has shown that the contraction of the muscle fibers is due to the possession by these fibers of certain very definite functions: the functions of rhythmicity, excitability, conductivity, contractility, and tonicity. All the fibers of the heart are not equally endowed with the same functions, some fibers being naturally endowed with those functions which are essential to the playing of their part in the mechanism of the heart. Thus some fibers have the power of contractility more developed than others, for it is evident that the muscle fibers constituting the apex of the heart must have different functions to perform than those that support the auriculoventricular valves. In the latter case the function of tonicity is naturally that one that would subserve the purpose of these fibers. It follows, then, that if the muscle fibers that prevent the regurgitation of the blood from the right heart into the great veins have their tonicity affected, they cannot effectively assist in closing the caval and tricuspid orifices. Keith has shown that this regurgitation during auricular systole is prevented by the contraction of a band of muscle in the auricular wall (the tænia terminalis), which shuts off the auricle from the superior vena cava. In some of the hearts I have sent him he has found these fibers elongated and attenuated, and during life there was great regurgitation of the blood into the veins during the heart's contraction. In like manner the fibers that support the tricuspid valves are very apt to lose their tonicity, and as these valves even in health are barely sufficient to close the

[2] The Evolution and Action of Certain Muscular Structures of the Heart, The Lancet, February 27, 1904.

[3] The Contraction of Cardiac Muscle, in Schäfer's Text-book of Physiology.

tricuspid orifice, the slightest depression of the tonicity of the muscle fibers at once permits regurgitation from ventricle to auricle.

TRICUSPID REGURGITATION. When I had taken tracings of the venous pulse and considered all the possible factors in its production, I took into consideration the fact that tricuspid regurgitation might play a very important part in the pulsation of the veins. Although its effects had been recognized in producing the so-called pathological venous pulse, no attempt had been made to show the connection between the so-called normal and the pathological venous pulses. That tricuspid regurgitation was the cause of the latter form was recognized, but no one had worked out how this tricuspid regurgitation began and gradually increased. Watching many cases and observing the signs of tricuspid regurgitation during life, and examining the hearts after death, I found abundant evidence that tricuspid regurgitation does modify even the so-called normal venous pulse. That my views were accepted by my colleagues in Britain was due to the fact that tricuspid incompetency is looked upon as so common, and so readily set up, that the whole train of my reasoning was conformable to their experience. But to my surprise I found that outside the British Isles my explanation was not accepted, as the fact that tricuspid incompetence was so easily set up had never been recognized.

Clinicians one hundred years ago, and John Hunter before them, recognized this tendency to incompetency of the tricuspid valves, but it was left to Wilkinson King,[4] in 1837, to demonstrate the relative natural incompetency of the tricuspid valves by a series of careful dissections and experiments. For several generations this has been the teaching in British schools, and in such text-books as those of Bramwell and Gibson the natural tendency to tricuspid incompetence is duly recognized. On the other hand, Babcock expresses surprise that Gibson should describe tricuspid regurgitation as a frequent occurrence, and, as an additional evidence of American opinion, Preble[5] recently bears testimony that tricuspid regurgitation is rarely recognized, and in citing some cases of pernicious anemia, he describes as new what has been taught in our schools for generations. Writers like Riegel, Krehl, Sahli, and others recognize tricuspid regurgitation when it is secondary to failure of the left heart, and in the extreme form when it produces the pathological or positive venous pulse. I have again carefully gone into the whole matter and made a series of new observations, noting the symptoms during life (particularly a murmur, systolic in time, heard loudest over the middle of the sternum, and over the third and fourth left costal cartilages), and I have followed certain patients until their death, and examined their hearts and found marked

[4] The Safety-valve Function in the Right Ventricle of the Human Heart, Guy's Hospital Reports, 1837, ii, 132.

[5] AMER. JOUR. MED. SCI., 1906, cxxxii, 393.

dilatation of the tricuspid orifice. But as even these cases might not be considered free from doubt, inasmuch as it could be held that the tricuspid dilatation was due to the changes taking place immediately preceding death, I have carefully noted the symptoms during life in patients whose tricuspid valves had been damaged by old-standing endocarditis. In these cases it would have been impossible for the valves to close efficiently, and regurgitation must have taken place. The results of my observations, as I will show, demonstrate that tricuspid regurgitation must have been a factor in producing the wave *v* in the auricular venous pulse in these cases.

METHODS OF RECORDING THE MOVEMENTS OF THE CIRCULATION. The examination is best carried out with the patient lying down, with the shoulders slightly raised, and the head comfortably supported by a pillow, so that the sternomastoid muscle can easily be relaxed. A great variety of movements may be observed in different patients.

There are several ways of taking tracings of the movements in the jugular vein. Usually the movements are recorded on the blackened paper of a revolving drum or of a sphygmograph at the same time as some other standard movement, such as the apex beat or arterial pulse. These methods, besides being troublesome, permit only of tracings being taken for a short period, and it is often necessary in the study of irregularities to take tracings extending over a considerable time. I have lately devised a method whereby the lever of the instrument writes, with ink, on paper that is unwound from a roll, so that tracings many yards in length can be taken with much less trouble. For taking movements of the jugular and the carotid pulses or of the apex beat I employ a shallow cup (receiver). When this is applied over the pulsating part in such a manner that all communication with the outer air is prevented, the movement of the air within the receiver is conveyed by an India-rubber tube to the tambour. I have devised a special arrangement for taking a tracing of the radial pulse: the knob on the membrane of a broad tambour rests on a steel spring which is moved by the radial pulse, the steel spring being in a splint which is strapped to the wrist. A time marker, driven by a separate clockwork, records one-fifth of a second. Most of the tracings for this paper have been taken by this method.[6]

For the due appreciation of the movements in the jugular vein it is absolutely necessary that, along with the jugular pulse, the movements of some event whose position in the cardiac cycle is known, be taken at the same time as a standard, by which to determine the position in the cardiac cycle of any movement in the jugular pulse. For this purpose the arterial pulse usually offers the most convenient movement. Its cause—ventricular systole—is absolutely

[6] This instrument is made by Mr. S. Shaw, watchmaker, Padiham, Lancashire, England.

determined. Fig. 1 shows the movements which serve as standards for the interpretation of a jugular pulse. I have placed below the jugular pulse, movements representing the apex beat and the carotid and radial pulses to show the relation in time of certain events in these various movements. The numbered down strokes indicate the time relations of the events in the jugular pulse, the apex beat, the carotid and the radial pulses: (1) The beginning of auricular systole; (2) the beginning of ventricular systole; (3) the opening of the semilunar valves and the appearance of the carotid pulse; (4) the beginning of the radial pulse; (5) the closing of the semilunar valves; and (6) the opening of the tricuspid valves. The space *E* between 3 and 5 indicates the time when the semilunar valves are open. These numbered down strokes and the space *E* have the same significance in all the other tracings. The time marked here and in all the other tracings equals one-fifth of a second.

FIG. 1.—Tracings of the radial, carotid, and jugular pulses and of the apex beat.

Although the carotid pulse and the apex beat can sometimes be usefully employed as a standard, it will be found that the radial pulse is, on the whole, the most convenient. A certain loss of time takes place in the transmission of the wave to the radial pulse, and this can be estimated by taking simultaneously with the radial a few beats of the carotid, as in Figs. 2 and 10, in which the space between 3 and 4 shows the loss of time between the appearance of the carotid and the radial pulses. This loss being allowed for, one can always find a definite period in a jugular tracing which corresponds to any event occurring in the neck due to the ventricular systole. I also employ a very useful period, namely, that portion of the ventricular systole during which the semilunar valves are open (period marked *E* in all the tracings). Its duration can be found in the radial tracing, extending from the beginning of the up stroke to near the bottom of the dicrotic notch. It corresponds to the time between the down strokes 3 and 5 in all the carotid, jugular, and apex tracings given here. In the neck the period *E* begins with the carotid pulse.

There is a slight delay between the opening of the aortic valves and the carotid pulse, but it is so short ($\frac{1}{50}$ of a second) that it may be ignored. The space *E* in the radial tracing is about one-tenth of a second behind the same period in the neck.

Another standard which I will be able to point out later is that of the opening of the tricuspid valves (downstroke 6 in all the tracings), which in jugular tracings is always indicated by the beginning of the fall of the wave *v*. In the apex tracing this event occurs at the bottom of the fall after the systolic plateau as in Figs. 22 and 23.

INTERPRETATION OF A JUGULAR TRACING. 1. *The Auricular Wave* (*a*). To interpret such a tracing as Fig. 2 we find the space *E* (that is the period during which the semilunar valves are open). There is a wave *a* immediately preceding this period. From its position in the cardiac cycle this wave can only have been due to the auricular systole. Although it is recognized as being due to the systole of the auricle, there is some doubt as to its manner of production.

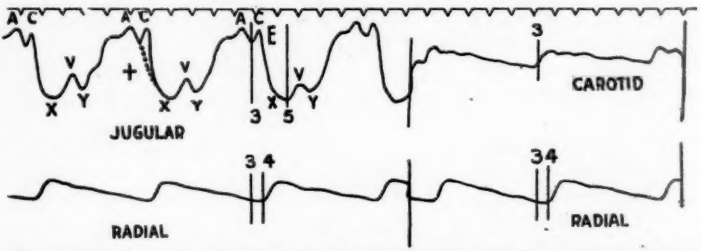

FIG 2.—Simultaneous tracings of the jugular and the radial pulses in the first part of the tracing and of the carotid and the radial in the latter part. The jugular pulse is of the auricular type. *a*, auricular wave; *c*, the carotid wave; *v*, the ventricular wave; *x*, the auricular depression; *y*, the ventricular depression. These letters have the same significance in all the other tracings.

Thus, it has been said to be due: (1) To a damming of the blood in the vein while the auricle is in systole; (2) to the fact that when an on-flowing stream is suddenly stopped there immediately takes place a wave in a contrary direction; and (3) to a true regurgitant wave. This is really a matter of some moment, as a due appreciation of this wave helps materially in understanding certain movements of the heart. Keith, as I have remarked, has described that regurgitation is prevented by the closure of the superior vena cava by the muscular band, the tænia terminalis. If the tonicity of this bundle be affected it will lengthen and become less effective. I am disposed to consider that it becomes readily affected by distention of the auricle under certain circumstances, even if it is ever really competent. In some of my cases in which there was a marked venous pulse, Keith has found this bundle greatly lengthened and atrophied, and I would therefore suggest that this wave is a true regurgitation wave and that it is due to inefficiency of the contraction

of the tænia terminalis. I may point out in support of this view that Chauveau and Faivre[7] found in the horse that normally there is a slight regurgitation during auricular systole, which becomes markedly increased when the breathing is stopped.

2. *The Auricular Depression* (x). After the auricular systole there is a fall (x in all the tracings). It is usually the greatest depression in a tracing of the auricular form of venous pulse. If we leave out, for the moment, the consideration of the wave c, and consider the fall as following the dotted line at + in Figs. 1, 2, and 22, this fall will be found to occupy the whole period of E in many of the tracings, while in others it stops at varying periods before the end of E (Figs. 10, 12, 14, etc.). This fall is due to three factors, of which the first and principal is the relaxation of the auricle after its contraction, whereby the blood in the vein is suddenly passed into the dilating auricle. As a rule, it cannot be said how much is due to this factor and how much to the other factors, but in exceptional instances, in which we get a delay in the appearance of the ventricular systole, we find this fall divided in two, as (x and x^1) in Fig. 13.

After the auricular systole in this tracing, there is a slight delay before the wave c appears, and the fall x, between a and c, is due to the auricular diastole. The period E marks the time of ventricular systole, and we find, during this period, that there is another fall x.[1] The cause of x^1 is, as was first pointed out by John Hunter, the diminution of the intrathoracic pressure, caused by the expulsion out of the chest of the blood by ventricular systole. It is this diminished intrathoracic pressure, which causes the aspiration of the air in the respiratory tract, which has been studied by Mosso, Landois, François-Franck, Delépine, and others. There is no doubt that it must also have some effect on the flow of blood in the veins and in producing the fall x^1 in Fig. 13.

Keith has pointed out to me that another factor would be the enlargement of the auricular cavity by the dragging down of the auricular-ventricular septum during ventricular systole. Chauveau had previously described a similar action, and probably it is a factor in the production of this fall. In a tracing from a case of heart block Wenckebach[8] has also demonstrated a division of this fall and gives an explanation similar to this.

3. *The Carotid Wave* (c). The carotid wave c gave rise to much discussion in the earlier days, but I was able to demonstrate, in 1893, that it is really due to the impact of the carotid on the air in the receiver, and is not due to a wave in the vein. I was able to produce such ample evidence that this interpretation was generally

[7] Nouvelles recherches expérimentales sur les mouvements et les bruits normaux du cœur. Gazette médicale de Paris, 1856, v, 406.

[8] Beiträge zur Kentniss der menschlichen Herstätigheit, Archiv f. Anatomie und Physiologie, 1906, 297.

accepted, but I find that Hirschfelder[9] and Morrow[10] have recently revived the old notion that it is in some way due to a wave sent back by the ventricle into the jugular vein.

It can be proved in many ways to be due to the carotid. Thus its synchronism with the carotid pulse is seen in Fig. 3. Clinically, we can demonstrate the nature of this wave by taking tracings from the neck at various levels. As we ascend higher in the neck the jugular element in the tracing will gradually disappear, while the carotid element will increase until nothing but the characteristic carotid pulse is left in the tracing. I have demonstrated this fact in many other ways, as, for instance, its absence when the jugular

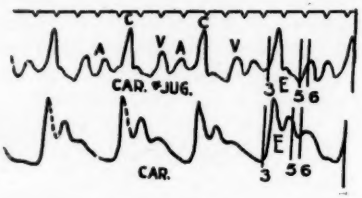

FIG. 3.—Simultaneous tracing of the jugular and the carotid pulses to show the synchronism of the wave c in the jugular with the carotid pulse.

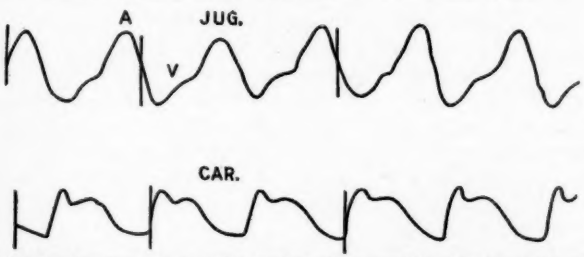

FIG. 4.—Simultaneous tracings of the jugular and the carotid pulses from a dog when the jugular had been dissected away from the carotid, showing the absence of a carotid wave in the jugular tracing (Cushny and Grosh).

wave is large, as in Fig. 8, and its absence from the auricular liver pulse, as in Fig. 9. Morrow reckons to have demonstrated experimentally that this wave is due to the ventricular systole, but I am disposed to think that his experiments are not reliable. At all events, when able experimenters like Cushny and Hering took pure tracings of the jugular pulse they were able to get a tracing without a carotid wave.

Fig. 4 shows a jugular tracing from a dog taken by Cushny and Grosh after they had dissected the jugular vein away from the carotid.

[9] Graphic Methods in the Study of Cardiac Disease, AMER. JOUR. MED. SCI., 1906, cxxxii, 378.

[10] Discussion on Heart Block, Brit. Med. Jour., October 27, 1906, and The Various Forms of the Negative or Physiological Venous Pulse, Brit. Med. Jour., December 22, 1906.

It will be seen that there is no wave in the jugular tracing at the time of the ventricular systole, although in tracings taken prior to this dissection the carotid wave was always present. Likewise, Hering's[11] tracings, after he had detached the vein from the carotid, showed no sign of a wave at this time.

4. *The Ventricular Wave* (*v*). The next event to be considered is the wave marked *v* in all these tracings. It will be observed that I mark with *v* the small wave occupying a very short period in the cardiac cycle, in Figs. 1 and 22, as well as the large wave in Fig. 23, for the reason that the smaller wave is but the beginning of the larger. The best way to study this wave is to begin at its end. What causes the fall that terminates it? If careful measurements be taken to find in what portion of the cardiac cycle the fall occurs, the beginning of the fall will be found to occur at the time of the opening of the tricuspid valves (6 in all the figures). As a matter of fact, the fall of this wave is due to the opening of the tricuspid valves, permitting the blood that has been stored in the auricle during ventricular systole to flow into the ventricle, thus emptying the jugular vein. If this fact be kept carefully in mind, the real significance of the wave *v* becomes clear; its cessation marks a very definite period in the cardiac cycle and forms a valuable standard in the interpretation of many obscure tracings. The manner of origin of this wave is as follows: While the pressure in the ventricle during ventricular systole is higher than that in the auricle, the tricuspid valves will remain closed. The flow of blood into the auricle will continue to accumulate until the auricle is filled and the overplus will be stored in the venæ cavæ and adjacent veins. When the overplus is sufficiently great it will appear in the jugular as a wave. If the overplus is slight the capacious vena cava may retain it all, so that it will not appear in the jugular before the tricuspid valves are opened. The greater the overfilling of the auricle and the veins the earlier will be the appearance of the wave in the period *E* of ventricular systole.

The question is, Whence comes the blood that produces this filling and overfilling of the auricle? In the majority of people the jugular pulse is only apparent when the individual is recumbent. This posture favors the flow to the heart from the abdominal veins, and in certain circumstances this seems readily to lead to overfilling of the right heart. Another source to be considered is the regurgitation back from the right ventricle. I have examined very carefully the state of the heart in several thousands of patients who had a jugular pulse, and I have found that in many of them I could detect a tricuspid systolic murmur and slight dilatation of the right heart. If regurgitation does take place, in what way will it affect the jugular pulse? If the amount be slight it will only cause an earlier filling

[11] Die Verzeichnung des Venenpulses am isolierten, kunstlich durchströmten Säugethierherzen, Archiv f. die ges. Physiologie, 1904, cvi.

of the auricle, and this may be only sufficient to cause the overfilling to extend as far as the jugular, causing a wave to appear just before the opening of the tricuspid valves between the down strokes 5 and 6, as in Figs. 5 and 22. If, on the other hand, the regurgitation be more free the filling of the auricle will occur sooner and the wave appear earlier in the jugular tracing. This is, as a matter of fact, what I have found to take place.

Fig. 5 is from a man suffering from shortness of breath and tightness across the chest, in consequence of a very laborious occupation. There was slight enlargement of the heart and a well-marked tricuspid systolic murmur. Fig. 6 is from a profoundly anemic woman,

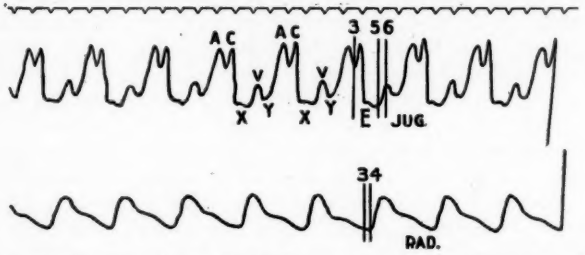

FIG. 5.—Simultaneous tracings of the jugular and the radial pulses from a man with tricuspid regurgitation. The jugular pulse is of the auricular type and shows a small wave after the period *E*.

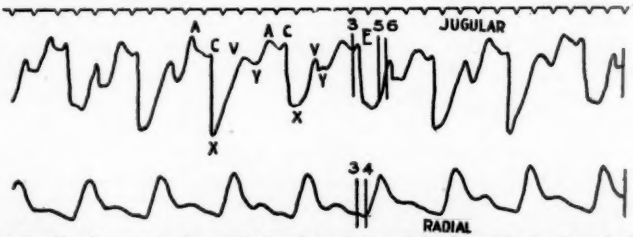

FIG. 6.—Simultaneous tracings of the jugular and the radial pulses. The jugular pulse is of the auricular type. From a profoundly anemic woman with marked tricuspid regurgitation.

with a large heart and a loud tricuspid systolic murmur, in whom there was a large pulsation in the veins of the neck. I have followed patients similar to these until they died, and found postmortem evidences of great dilatation of the tricuspid orifice.

Thus, Fig. 7 is from a man who suffered from pernicious anemia. There was slight enlargement of the heart and a tricuspid systolic murmur. He died, and on postmortem examination the tricuspid orifice readily permitted the passage of four fingers. In such cases I suggest that the depressed tonicity of the muscular ring supporting the tricuspid valves permitted enlargement of the orifice and consequent incompetence of the tricuspid valves.

As some doubt may even here exist in regard to the diagnosis, I would call attention to instances of undoubted tricuspid regurgitation in patients in whom the tricuspid valve had been partially destroyed as a result of old endocarditis, and in which there could be no doubt of the fact that tricuspid regurgitation had occurred during life. I

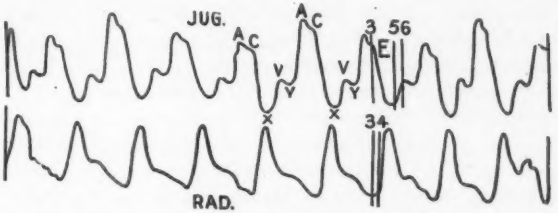

FIG. 7.—Simultaneous tracings of the jugular and the radial pulses from a man suffering from pernicious anemia. At the postmortem examination the tricuspid orifice was widely dilated. The jugular pulse is of the auricular type.

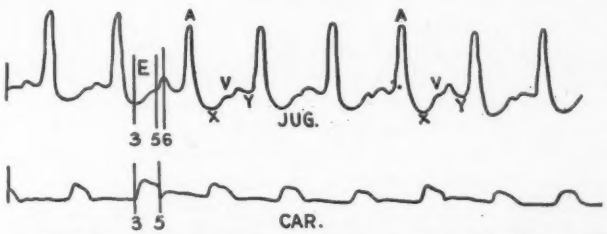

FIG. 8.—Simultaneous tracing of the jugular and the carotid pulses from a patient in whom the tricuspid valves were found damaged by an old endocarditic process, and the tricuspid orifice thereby rendered markedly incompetent. The jugular pulse is of the auricular type.

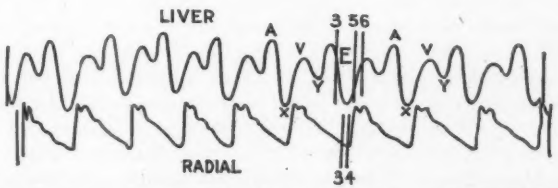

FIG. 9.—Simultaneous tracing of the liver pulse and the radial pulse from another patient whose tricuspid valve had been rendered incompetent because of an old endocarditis. The liver pulse is of the auricular type.

have had postmortem examinations on 8 cases of moderate tricuspid stenosis in which the opening permitted the passage of one or two fingers; in 6 of these there was pulsation of the auricular form in the jugular vein and the liver, and I had taken a large number of tracings of these pulsations.

Fig. 8 is a tracing of the jugular pulse from one case, and Fig. 9

is a tracing of the liver pulse from another. In an analysis of these tracings it will be found that the wave *v* is small and appears only toward the end of ventricular systole, and its fall begins at the time of the opening of the tricuspid valves. That is to say, in the people from whom these tracings were taken, tricuspid regurgitation undoubtedly occurred, and in doing so it must have modified the wave *v* in the tracings. I cannot conceive how it could affect these tracings in any way other than in participating in the earlier filling of the auricles and veins and, therefore, in the production of the wave *v*.

I have selected purposely, to illustrate my argument, cases in which there could be no reasonable doubt as to the occurrence of tricuspid regurgitation, in order to impress the fact that this factor must be concerned in the production of the wave *v*. As I have said, I have taken tracings of several thousand cases and have studied at the same time the condition of the heart. In the large majority of cases no tricuspid murmur could be heard, and in many cases there was practically no increase in the size of the heart.

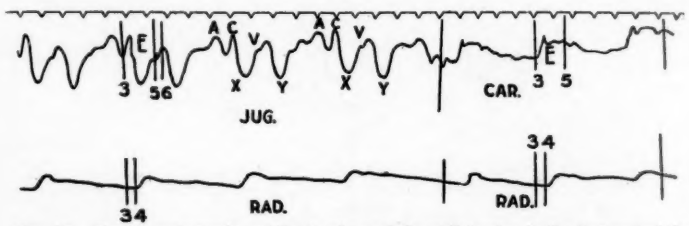

FIG. 10.—Simultaneous tracing of the jugular and the radial pulses in the first part of the tracing, and of the carotid and the radial pulses in the latter part. From a man without a tricuspid systolic murmur.

Thus, Fig. 10 was taken from a pale, spare man, aged twenty-five years, with dilated stomach. There was no cardiac enlargement and no systolic murmur. He was rather short-winded. The wave *v* encroaches on the period *E*. What is the explanation of such cases? Tricuspid regurgitation is not excluded by the absence of a systolic murmur. One can frequently demonstrate the existence of large tricuspid regurgitation, as shown by a ventricular venous pulse, with the absence of a tricuspid regurgitant murmur. Careful clinicians are well aware that under certain circumstances regurgitation can occur at all the orifices with no murmur. Thus, for instance, in the enormously dilated hearts of adherent mediastinitis there may be no systolic murmur though the mitral and tricuspid orifices are greatly widened. The question, therefore, whether tricuspid regurgitation takes place in such cases as the man from whom Fig. 10 was taken is one on which I have not sufficient evidence to decide. As I have already pointed out, the essential element in the production of the wave *v* is a sufficient accumulation of blood in the right auricle,

so that the auricle and superior vena cava are overfilled during the period of the cardiac cycle when the tricuspid valves are closed. This can occur with a slight engorgement of the right heart, when there is an increase in the residual blood after the auricular systole. The jugular pulse in these cases readily disappears with more rapid action of the heart, as on moderate exertion, or on the supervention of a slight febrile attack, and often increases in size with a slower action of the heart. It is probable the mere increase of the accumulated blood in the right heart may suffice alone to produce the wave *v* in such cases, but whether it may at the same time render the tricuspid valve incompetent is a question that must be considered, but which I am unable to answer.

Before demonstrating how the auricular venous pulse passes into the ventricular, I will consider some of the objections raised against the foregoing explanation. The erroneous notion very commonly raised by people who have not fully considered all the factors concerned and found in text-books, physiological and clinical, is that if there were tricuspid regurgitation in such cases as in the foregoing instances the wave *v* ought to appear at the beginning of ventricular systole and not at the end. If the jugular vein was in such direct communication with the right ventricle as the carotid is with the left, then undoubtedly the wave *v* should appear at the same time as the carotid. *But it must be borne in mind that between the right ventricle and the jugular vein there is interposed a dilating auricle and a capacious superior vena cava, and that a wave can only appear in the jugular after the auricle and vena cava have been overfilled.* It is for this reason that the time of the appearance of the wave *v* in the period *E* is a measure of the engorgement of the right auricle, as I shall demonstrate shortly.

It has been suggested by Gerhardt, Wenckebach, and others that the wave *v* in such tracings as Figs. 2 and 5 is due to a backward movement of the auriculo-ventricular septum after the closure of the semilunar valves. They state that at this period, when relaxation of the ventricle takes place, the septum swings back, sending a wave through the auricle and superior vena cava into the jugular. I am too ignorant of the movements of the heart to say whether there is such a movement at this time, and the arguments given in favor of it are more presumptive than demonstrative. Admitting, however, that it does occur, it would only be a factor added to those I have already given, and would not account for the portion of the wave occurring during the period *E* in such tracings as Fig. 10. I called attention, in 1893, to the fact that there is often a notch in the jugular tracing at the time of the closure of the semilunar valves, but its cause is still obscure. If this return of the auriculoventricular septum does take place it cannot be of such great force, as, for instance, to distend the liver and raise one's hand when laid on the liver, for one can see the hand raised by this wave, in palpating the liver in cases of

auricular pulsation of that organ. Another curious feature is that those who support this view leave out of consideration altogether the manner in which this wave *v* grows forward into the period *E*. Lately two physiologists, Hering and Morrow, by experiments on dogs, have sought to show that this wave is a normal sign and has nothing to do with tricuspid regurgitation. Their experiments are not conclusive, for they do not seem to have tested whether the tricuspid valves were competent, nor did they seek to produce tricuspid incompetence and observe the result on such incompetence. I do not see how they can say that tricuspid incompetence did not participate in the production of the waves in the cases cited here when the tricuspid valves were damaged.

5. *The Ventricular Depression* (*y*). The next event after the wave *v* to be seen in the jugular and liver pulsation is the fall marked *y* in all these tracings. Its cause is readily understood, being due to the passage into the ventricle of the blood stored in the auricle during ventricular systole. It will be noticed that in all these tracings the fall begins at the down stroke 6, that is at the time of the opening of

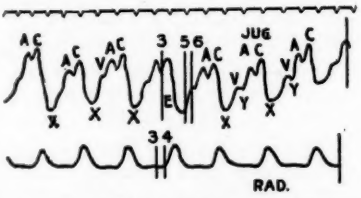

FIG. 11.—To show the disappearance of the fall *y* and the wave *v* with quickening of the heart rate.

the tricuspid valves. If the heart be slow in rate it is followed by a rise shown in Fig. 2, between *y* and *a*. This rise is due to stasis in the veins. If the heart quickens in its action the period of stasis first disappears and the fall *y* is followed at once by the auricular wave. If further quickening occurs the fall *y* disappears from the tracing, and the wave *v* becomes continuous with the auricular wave, as in Fig. 11.

In my book on the pulse I have given numerous illustrations of these features, so that I need not dwell on them here. As a rule, the fall *x* is more marked than the fall *y*, in the auricular form of the venous pulse; but, as the pulsation passes into the ventricular form the fall *y* gradually becomes the more pronounced, and the fall *x* diminishes, until it disappears altogether, until there is but one large wave synchronous with and due to the ventricular systole, and one great fall *y*, synchronous with and due to the ventricular diastole. The manner in which this occurs I will now proceed to demonstrate.

THE PASSAGE OF THE AURICULAR FORM OF THE VENOUS PULSE INTO THE VENTRICULAR. The reason I called the wave marked *v* the

ventricular wave in the foregoing tracings, although it may be that the ventricular systole in many instances takes no part in its production by sending blood back into the auricle, was to impress the fact that had been overlooked, that tricuspid regurgitation must have had a beginning, and that the "positive" or ventricular jugular pulse, which everyone recognizes as due to extreme tricuspid regurgitation, began its appearance as a small wave appearing at the end of ventricular systole. How necessary it was to insist on this fact is seen in the writings of those who have not recognized early tricuspid regurgitation. Scarcely a writer ever attempts to explain how the "positive" venous pulse comes about. The reason for this silence is, that these writers, clinicians as well as physiologists, have failed to recognize the important factor of slight and moderate tricuspid regurgitation. I quite admit that to follow my argument it may require a clearer exposition than I am capable of giving, but my acts cannot be gainsaid. If, therefore, those interested in this matter will ponder deeply on this somewhat complex problem, I am convinced they will see the explanation as clearly as I do.

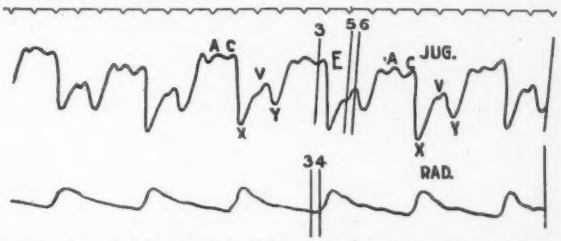

FIG. 12.—Shows the extension forward of the wave *v* into the period *E* when the patient held his breath. Compare with Fig. 5, taken from the same patient.

While the following explanation shows how the auricular form of the venous pulse passes into the ventricular, it affords, at the same time, proof of varying degrees of engorgement of the right heart and demonstrates the manner in which an increasing engorgement can be recognized in tracings of the jugular pulse. I am somewhat at a loss in selecting illustrations, as no two cases are alike in all particulars, and I have by me such an abundance of material illustrating the view I am propounding, that in the limits of this paper I am restricted to giving only a very small portion of my proofs. In suitable cases it is possible to increase the amount of right-heart engorgement by getting the patient to hold his breath. In many instances in which the jugular pulse is of the ventricular type, it may occasionally disappear, but can be brought back by holding the breath. In some cases in which the jugular pulse is of the auricular form the wave *v* can be made to increase in size and to appear earlier in the cardiac cycle by the same method. Thus, Fig. 5 shows *v* appearing only after the period *E*. When I told this patient to hold his breath

for a long time the jugular pulse increased in size and the wave-*v* extended forward into the period *E*, as in Fig. 12.

Here I reason that the greater resistance offered to the systole of the right ventricle by the cessation of the breathing had caused a rise in the ventricular pressure and an increased backward flow. This explanation corresponds with that of Hering's[12] experiment when he found he had difficulty in raising the pressure in the right ventricle, because of the ease with which the tricuspid leaked.

The best evidence of increasing engorgement is to be found by watching individual cases for many years and noting the gradual

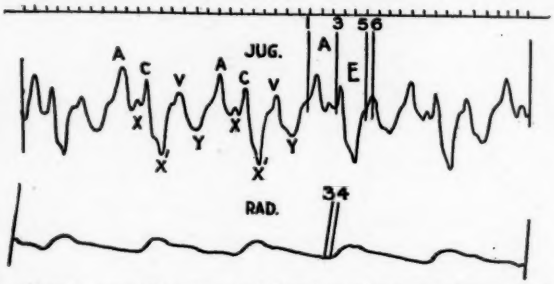

FIG. 13.—Note the size of the wave *v* in this and the following tracings. W. H., 1892.

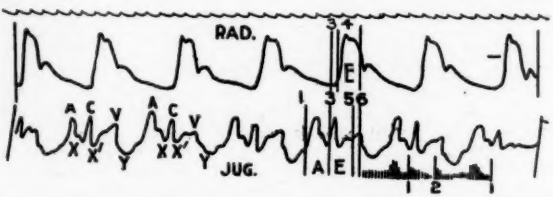

FIG. 14.—The shading underneath the jugular tracing shows the position of the heart murmurs. 1 and 2 refer to the first and second sounds. Note the increase of the diastolic murmur at the time of the auricular systole. W. H., 1903.

advance of the cardiac inefficiency. The following case is a good illustration of this method: I attended a man during an attack of acute endocarditis, in 1881, he then being thirty-two years of age. He was left with a mitral regurgitant murmur. In my notes of his case I find a tracing of his jugular pulse taken in 1892 (Fig. 13), which shows that the wave *v* began a little before the end of the period *E*. At that time he was in fair health. It will be noted in the tracings from this patient that the carotid wave *c* follows the wave *a* at a greater interval than in the other tracings of the jugular pulse given in this paper. This delay implies a depression of conductivity of the fibers joining auricle and ventricle. In some tracings,

[12] Zur experimentellen Analyse der Unregelmässigkeiten des Herzschlages. Archiv f. die ges. Physiologie, Bonn, 1900, lxxxii.

taken in 1897, I find this had increased so much that there was a slight heart block. In 1898 he suffered from an attack of grievous heart failure, from which his recovery was slow and protracted. In 1903, I took the tracing, Fig. 14. Here it will be noted that the wave *v* appears still earlier in the period *E*. At this time there was, in addition to the mitral systolic murmur, a long diastolic murmur with a curious increase of intensity a little before the first sound, a brief interval occurring between this increase and the first sound, corresponding to the shading underneath the jugular tracing. It will be seen that the rise in the shading occurs exactly at the time of the auricular systole. It was my custom to ask my colleagues when showing them this patient, to draw for me on a tracing the period

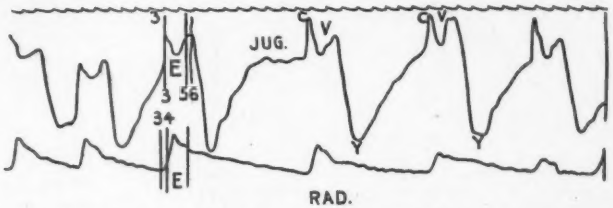

FIG. 15.—Simultaneous tracing of the jugular and the radial pulses. Note the irregularity and the absence of an auricular wave as compared with Figs. 13 and 14. The jugular pulse is now of the ventricular type. W. H., April 6, 1904.

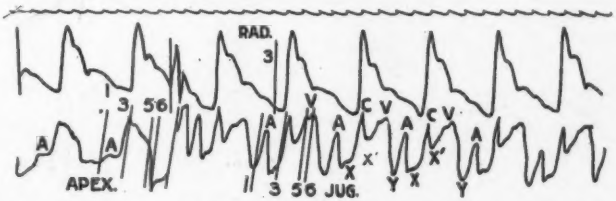

FIG. 16.—Simultaneous tracings of the radial pulse and the apex beat in the first part of the tracing and of the radial and the jugular pulses in the latter part. The pulse is again regular and the auricular wave *a* has returned to the apex beat and the jugular pulse. W. H., April 11, 1904.

in the cardiac cycle in which this increase in the intensity of the diastolic murmur occurred, and in every instance they placed the period of increase exactly where I have shown it, although they could form at the time no opinion as to the cause of the increase. There can be no doubt that the increase in the loudness of the murmur at this time was due to the auricular systole.

The character of the jugular pulse on repeated examinations continued like Fig. 14 until April 6, 1904, when I found the pulse continuously irregular, and on listening to the heart there was a systolic and a diastolic murmur at the apex, but no increase in the diastolic murmur before the first sound. On taking a tracing all sign of the auricular wave had gone from the jugular pulse and there was but one large wave during the ventricular systole (Fig. 15). A

week later the pulse was found to be quite regular and the jugular tracing showed the auricular wave had returned (Fig. 16). At the beginning of this tracing there are a few beats from the apex which show a wave, due to the auricle. I have taken a large number of apex tracings and never failed to find this wave when the rhythm was regular. The heart continued quite regular until the month of August, 1904, when I found it again continuously irregular and it has remained thus ever since.

Figs. 17 and 18 were taken on December 9, 1906, and are typical of the form of arrhythmia that I have found in the numerous tracings I have taken during the last two years—one large wave synchronous

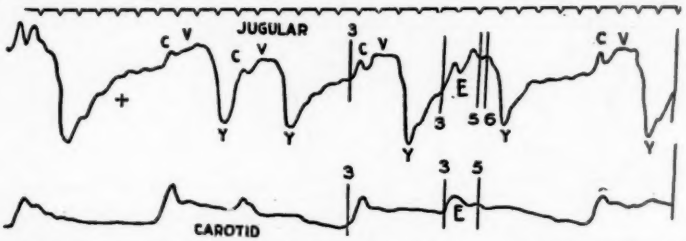

FIG. 17.—Simultaneous tracings of the jugular and the carotid pulses. The jugular pulse is now of the ventricular type. Note the irregularity and the small ripples in the tracing at the long pause +, due in all likelihood to fibrillary contraction of the auricle.

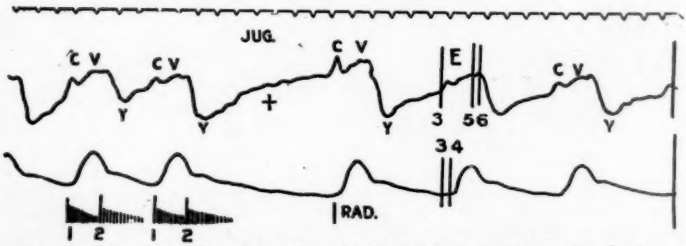

FIG. 18.—Here the jugular pulse is taken with the radial pulse and shows the same features as Fig. 17. Note the shading showing the murmurs and sounds of the heart, and compare with Fig. 14. W. H., 1906.

with the ventricular systole, no sign of an auricular wave in the tracing of the apex beat or the jugular pulse, no murmur due to the auricular systole, and invariably irregular. To appreciate more clearly the changes in the jugular pulse I arrange one cardiac cycle from Figs. 13, 14, 16, and 17, above one another, showing thus in a semi-diagrammatic form the gradual increase of the wave *v*, and bringing out clearly its meaning (Fig. 19). This demonstration of the passage of the auricular form of the venous pulse into the ventricular justifies the names I have given them, for it is seen in these tracings that the disappearance of the auricular wave marks at once a remarkable

change not only in the character of the venous pulse but also in the rhythm of the heart. I wish to insist upon these facts, because though much has been written on mitral stenosis the clinical signs have never been properly appreciated, not even the fact that when the heart becomes continuously irregular, as it often does in advanced mitral stenosis, a presystolic murmur of the crescendo type

Fig. 19

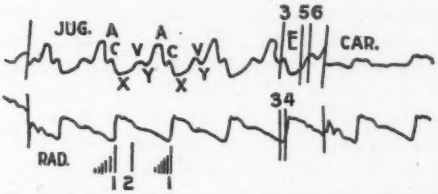

Fig. 20

Fig. 19.—Semidiagrammatic illustration of the passage of the auricular form of the venous pulse into the ventricular. Note the gradual increase in the size of the wave *v*.

Fig. 20 is from a case of mitral stenosis, taken in 1896, and shows a regular heart and a jugular pulse of the auricular form. The crescendo murmur is represented in the shading running up to the first sound. Mrs. P., 1896.

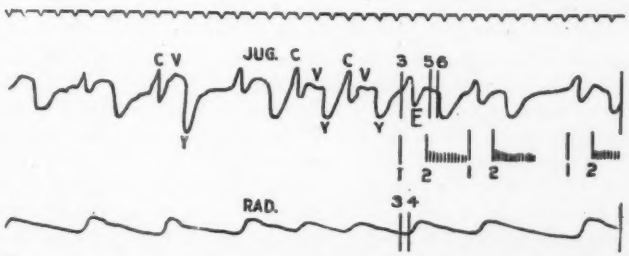

Fig. 21.—From the same patient as gave Fig. 20, taken in November, 1906. The rhythm is now irregular and the jugular pulse is of the ventricular type. The shading shows a diastolic murmur and an absence of the crescendo character represented in Fig. 20. Mrs. P., 1906.

is never heard. A diastolic murmur may be present and it may last during the whole of a short diastole, but if care be taken it will be found never to terminate in a crescendo murmur, and when the diastole is prolonged the murmur will be found to stop short of the first sound, as shown in the shading of Fig. 21.

Fig. 20 is a tracing taken in 1896, from a woman with mitral stenosis. The pulse is regular and the jugular shows the usual form

of auricular venous pulse. The shading shows the position of the crescendo presystolic murmur running up to the first sound. In 1900 her heart became irregular and has remained so ever since. Fig. 21 is a tracing taken in 1906, and is characteristic of the irregularity and type of venous pulse—the ventricular—that has been present the past six years.

When the patient's heart beats quickly, as after exertion or excitement, the rate being rapid, the rhythm is fairly regular and a diastolic murmur fills up the whole of the diastolic period and might be mistaken for a presystolic murmur. But there is no crescendo character present in it. When, however, the heart becomes quieter, the irregularity becomes more marked, and long diastolic pauses ensue, and then it will be found that the diastolic murmur does not fill up the whole diastolic interval but stops short, as shown in the shading of Fig. 21. I have been able to demonstrate this peculiarity in a great number of cases to many of my colleagues. The study of the jugular tracings at once reveals the reasons for these changes. Progressive narrowing gives rise to, first, a crescendo presystolic murmur, then there is added a diastolic murmur, then the auricle ceases to beat at its normal period of the cardiac cycle and the crescendo murmur disappears, and the heart becomes irregular. In advancing mitral stenosis, therefore, these events happen simultaneously: (1) Disappearance of the auricular wave from the jugular pulse and apex beat; (2) disappearance of the auricular systolic (crescendo presystolic) murmur; and (3) arrhythmia of the heart. So far as the venous pulse is concerned this means the change from the auricular form to the ventricular.

It so happened that my earlier cases of the ventricular form of the venous and the liver pulses were all secondary to disease of the mitral valve, and at the postmortem examinations I had found the right auricle enormously distended and the muscle fibers greatly atrophied, so that I surmised that the auricle, like an overdistended bladder, had become paralyzed. This view seemed to be confirmed by the results of careful observation of individual patients extending over many years, the auricle never putting in an appearance at its normal period in the hundreds of tracings I have taken. This view I expressed in my book, but when writing it a few cases came under my observation that gave me grounds for suspecting that "auricular paralysis" was not the only condition that gave rise to the ventricular form of the venous pulse.

I, therefore, started on an inquiry into all forms of arrhythmia, and collected a large number of cases. From among these I was able to differentiate a group of over 500 cases in which the irregularity was of a disorderly nature, as in Figs. 21 and 23. Over one-half of these cases had a venous pulse, and in every case it was of the ventricular form. In more than 50 cases the disorderly rhythm had started when the patient was under observation, and it invariably

meant the change from the auricular form to the ventricular—often suddenly. Usually, these cases for years have an occasional irregularity due to ventricular extrasystoles, that is, when the ventricle contracts before the auricle and independently of the stimulus from the auricle. I shall cite only one case as an illustration, particularly, as it has some historical value, being the first human subject in whom I demonstrated the nature of ventricular extra-systole.

In 1892, I took the tracing Fig. 22. In many tracings taken from this patient up to 1906 the venous pulse was always of the auricular form, as in this tracing, though she frequently showed ventricular extrasystoles, which are given in my book (Figs. 69 and 279). I saw her on August 6, 1906. The pulse had suddenly become quick

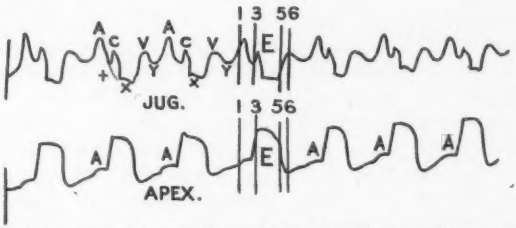

Fig. 22.—Simultaneous tracings of the jugular pulse and the apex beat. The jugular pulse is of the auricular type. Compare with Fig. 23. Mrs. A., 1892.

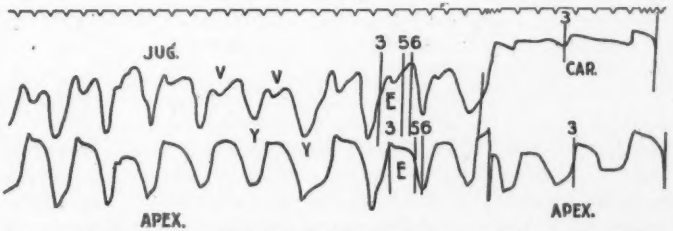

Fig. 23.—Simultaneous tracings of the jugular pulse and the apex beat. The jugular pulse is now of the ventricular type. Mrs. A., November, 1906.

and irregular and the jugular pulse was of the ventricular type. By November it had slowed down, and Fig. 23 is a characteristic tracing of its present condition.

Compare here the disorderly rhythm, the absence of the auricular wave in the jugular, and the apex tracing, with the perfect regularity and the presence of the auricular wave in the jugular and apex tracing of Fig. 22. Note, however, the persistence of the wave *v* between the down strokes 5 and 6 in both cases.

What is the auricle doing in cases with the ventricular venous pulse? I had assumed that it was paralyzed, and the total absence of any sign of its action for years, and the extreme distention of the chamber and its atrophied walls seemed to support the view. In

some cases I have found evidence that it contracts at the same time as the ventricle, and on postmortem examination these cases did not show extreme atrophy of the auricular muscle. In a few other cases I sometimes found a series of small waves on the ascending line of the tracing preceding the ventricular wave, as at + in Figs. 17 and 18. The waves are sometimes larger than those in these tracings, as at + in Fig. 24, which was taken from the same patient that gave Fig. 22 and 23.

In discussing this matter with Professor Cushny he said he had no hesitation in accepting the view that these small movements are due to fibrillary contraction of the auricle, as he had frequently witnessed the auricle in fibrillary contraction while the ventricle went at a slower rate.

One conclusion I have come to, and it is this, that when the ventricular venous pulse is present the heart's contraction proceeds no longer from the normal place, that is, at the mouths of the great veins, but probably at the fibers joining the auricle and the ventricle. At

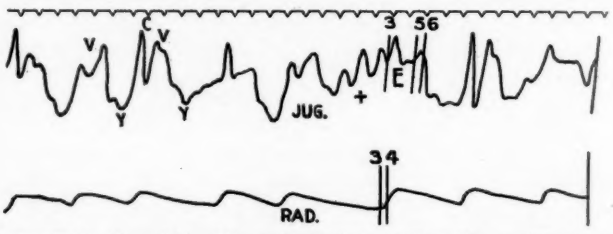

FIG. 24.—The jugular pulse is of the ventricular type and shows three small waves at + probably due to fibrillary contraction of the auricle.

present, Dr. Keith is conducting a minute inquiry into the condition of these fibers in a number of hearts I sent him of patients from whom, during life, I have taken numerous tracings, and so far it would seem that he will be able to show some anatomical facts justifying the foregoing conclusion. If this is so it will throw a flood of light on many obscure cases of heart failure which are at present buried under such vague terms as "chronic myocarditis," "fatty heart," "mitral irregularity," etc. It opens up a new view to clinicians and physiologists, and its bearing on treatment is of the very greatest importance. The heart failure is directly due to the arrhythmia, for the parts of the heart no longer work in that orderly manner designed by nature; consequently, treatment has a very definite aim before it. Further, the effect on these hearts of such a drug as digitalis is entirely different from the effect on a heart beating with a normal rhythm.

I hope that I have been able to show how necessary it is for the proper appreciation of the functional pathology of the heart, to understand the meaning of the venous pulse, and also to show that a great field for research still lies before the student of clinical medicine.

BACTERIAL INOCULATION IN THE TREATMENT OF LOCALIZED INFECTIONS.

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(From the Pathological Laboratory of the Montreal General Hospital, Montreal, Canada.)

In June, 1906, the necessary equipment was installed in the Pathological Laboratory of the Montreal General Hospital for the prosecution of research and clinical work in the field of bacterial inoculation, after a first-hand experience by one of us in the laboratory of Professor A. E. Wright, at St. Mary's Hospital, London. Ample material was promptly placed at our disposal, and from a series of upward of fifty cases a selection based upon the following considerations has been made: (1) Cases yielding the most brilliant results from the point of view of the time required to effect a cure, and (2) cases representative of different infections or varying clinical types of the same infection.

Technique of the Method of Preparing Bacterial Vaccines. The method here described in detail applies to the preparation of vaccines from the staphylococcus group. For variations as to media, age of cultures, devitalizing temperature, dosage, etc., one should consult the appended table and special remarks.

In cases of acne and furunculosis material for cultural purposes is obtained by puncturing the lesion with a sterilized needle, after washing the cutaneous surface with alcohol and ether. The pus expressed is transferred by the aid of a platinum loop to a plain agar slant, care being taken to ensure an even distribution of the material over the entire surface. This may best be effected by employing several loopfuls of the water of condensation. In order to secure the highest efficiency it is desirable that the vaccines be prepared from the original cultures or from first transplants.

After incubation for from twelve to eighteen hours the growth, if in pure culture, is washed from the surface of the slant with 6 c.c. of 0.85 per cent. saline solution, and decanted into a sterile test tube. The tube is then drawn out and sealed in the blowpipe flame and the contents agitated for ten minutes to ensure an even emulsion. The tube is then reopened, a drop of the emulsion for standardizing purposes is expelled, and the tube is resealed and immersed in the water-bath for one hour at 60° C. Finally a control culture is made and placed in the thermostat for twenty-four hours, at the end of which time, if negative, the vaccine may be diluted for use.

STANDARDIZING. Into a long narrow pipette fitted with a rubber teat and upon which a volume has been marked with a blue pencil, equal volumes of finger blood and the emulsion withdrawn before devitalization are aspirated, together with one or more volumes of 0.85 per cent. saline solution as a diluent. The contents of the pipette are then expelled upon a slide, thoroughly mixed by repeated aspiration, and films drawn. The latter are then stained by Leishmann's or Wright's blood stain and 500 red cells counted, noting at the same time the number of cocci present in the different fields. By a comparison of the two the number of cocci per cubic millimeter may be readily determined. Thus if in counting 500 red cells 500 cocci are encountered the vaccine contains 5,000,000 cocci per cubic millimeter or 5,000,000,000 per cubic centimeter.

DILUTING AND LYSOLIZING. For diluted vaccine 50 c.c. amber-glass bottles are employed. These bottles are filled with 50 c.c. of 0.85 per cent. saline solution, plugged with cotton-wool, and autoclaved. To continue our example of a vaccine standardized at 5,000,000,000 per cubic centimeter: After determining the cubic contents of the vaccine tube (or comparing it with a tube of equal size filled to the same level with water and measured) 5 c.c. of the contents of the bottle is poured into a cubic centimeter graduate, and replaced by an equal quantity of the concentrated vaccine. We thus have an emulsion 1 c.c. of which contains 500,000,000 staphylococci. We next add 0.25 per cent. of pure lysol—that is 2.5 milligrams per cubic centimeter. Finally a sterilized rubber cap is drawn over the neck of the bottle, and the mouth of the bottle immersed to the shoulder in hot paraffin. In withdrawing a vaccine for use the hypodermic needle is plunged through the rubber cap after sterilizing the surface in the flame. The puncture is closed by the same procedure. In calculating dilutions it is desirable that the minimum dose should not be less than 0.25 c.c.

SPECIAL REMARKS. While in order to save time the use of a "stock" vaccine may be employed, that is a vaccine prepared from the infective organism in a similar clinical condition, a "personal" or autogenous vaccine should be prepared from the infecting agent in each individual case if the best results are to be obtained. Personal vaccines of staphylococcic infections are chiefly of importance in the treatment of acne, whereas in furunculosis and carbuncle, heterogenous vaccines not infrequently yield surprising results.

In the treatment of staphylococcic infections apart from acne it has been our practice to employ for the initial dose a vaccine which has previously yielded prompt results in the treatment of lesions presenting similar clinical features; thus a "personal" vaccine prepared from a case of furunculosis may be subsequently employed as "stock" vaccine in the treatment of a similar clinical condition. The same remarks apply to sycosis, carbuncle, and impetigo infections.

In sinus infections the preparation of "personal" vaccines is

somewhat more complicated, as there are usually present in addition to Staphylococcus aureus and albus one or other of the large group of saprophytes, necessitating careful plating of the original culture. If Staphylococcus aureus and albus (or citreus) are present a mixed vaccine should be employed. The same laborious procedure is usually necessary in order to isolate the pneumococcus from the discharge of an empyemic cavity. In streptococcic infections the personal vaccine appears to be a *sine qua non*.

In Bacillus coli infections of the bladder there is seldom much difficulty in isolating the organism in pure culture, and in cases in which this organism alone is responsible for the symptoms, inoculation yields prompt results.

In meningococcal infections the value of the personal vaccine has not yet been demonstrated, but from our experience with gonococcal infections, if any analogy may be assumed, autogenous vaccines are, as a rule, the least effectual. So far we have employed but one strain of the meningococcus, with excellent results. In order to isolate this organism with reasonable certainty the cerebrospinal fluid obtained by lumbar puncture should be placed in the thermostat for twenty-four hours, then subjected to sedimentation in a high-speed centrifuge, and the residue transferred to blood-agar slants. By this means an abundant growth is usually obtained after twenty-four hours' incubation, even in cases in which numerous slides from the original fluid fail to show the presence of cocci. Vaccines should then be prepared from transplants, and incubated for from twelve to eighteen hours. The washings from several tubes may be employed if growths are scanty, but the use of young cultures is of paramount importance for accurate standardizing, as autolysis is usually early and rapid, so that vaccines prepared from old cultures may be of a strength out of all proportion to the numerical count.

In the preparation of gonococcal vaccines six-hour growths upon hydrocele-agar yield the best results. In older cultures it has been found impossible by simple agitation to obtain an even emulsion, in the absence of which standardization cannot be considered accurate owing to the presence of large clumps which do not permit of enumeration.

Tubercle Vaccine. In the treatment of localized tuberculous lesions we have heretofore employed Koch's T. R. tuberculin, which may be obtained in 1 c.c. containers, representing in suspension 10 milligrams of devitalized, dried, and ground tubercle bacilli. Dilution should be carried out in the following manner:

1. Immerse the container for ten minutes in pure lysol, wipe with a sterile towel, open, and decant into a standard vaccine bottle containing 39 c.c. of 0.85 per cent. saline solution, which has previously been autoclaved; rinse the container with 1 c.c. of fluid from the vaccine bottle; add to the whole 0.25 per cent. of pure lysol or 100 milligrams. Adjust the rubber cap and seal as before described. 1 c.c. of this

first dilution contains 0.25 milligram of tuberculin. This dilution is used as "stock."

2. After thoroughly shaking withdraw through the rubber cap by means of an accurately graduated syringe fitted with a hypodermic needle 1 c.c. of this "stock" dilution, and transfer it to a second vaccine bottle containing 49 c.c. of autoclaved saline solution, lysolize and seal as before. This dilution constitutes "Tuberculin No. 1," 1 c.c. of which contains $\frac{1}{200}$ milligram.

3. From this second dilution withdrawn by the same means 10 c.c. and add it to 30 c.c. of autoclaved saline solution contained in a third vaccine bottle. Lysolize by adding 75 milligrams of pure lysol. This third dilution constitutes "Tuberculin No. 2," 1 c.c. of which contains $\frac{1}{800}$ milligram of T. R. tuberculin.

It is of great importance that each step should be carried out with the strictest precautions against contamination and that each dilution should be carefully labelled so that the possibility of administering an overdose may be reduced to a minimum. The dose should be $\frac{1}{800}$ to $\frac{1}{2000}$ milligram according to body weight and the nature of the lesion. It is better practise to begin with a minimal dose, say $\frac{1}{1600}$ milligram, until the degree of reaction is known through subsequent determinations of the opsonic index, and when the negative phase is pronounced or prolonged or the patient complains of headache and general malaise it is well to adhere to the minimal dose for the first few inoculations. An exception to this rule of minimal primary dosage is, in our opinion, to be found in cases of infection of the urinary tract, in which the maximum dose, that is $\frac{1}{800}$ milligram, may be given at the first inoculation.

We have attempted the preparation of "personal" tuberculous vaccines employing the same general technique as for other organisms (see Case I) amplified as follows:

Cultures from bouillon flasks should be taken as soon as the growth has reached the margin of the fluid, that is before corrugation of the surface or precipitation has occurred. The cultures are first immersed in the water-bath for two hours at 60° C., in order to devitalize. The bouillon is next removed by siphon, and the residue washed in 0.85 per cent. saline solution, and centrifugated until the overlying fluid is perfectly clear. This fluid is then decanted and the mass of tubercle bacilli dislodged into a sterile agate mortar, where it is ground for one hour, sufficient saline being added from time to time to maintain a pappy consistence. This finally divided material is then diluted with 10 c.c. of saline solution, centrifugated for fifteen minutes to get rid of the clumps, and the supernatant emulsion is siphoned off into a sterile test tube. The residue is again ground, diluted, and centrifugated. This emulsion is added to that already obtained and the test tube is sealed and thoroughly agitated; after withdrawing a specimen for standardization, the vaccine is once more heated in the water-bath for two hours at 60° C. Finally this is diluted and lysolized. The minimal dose is 500,000.

While this method is open to certain objections, it is one which may be carried out by those in possession of a comparatively meagre laboratory equipment. Time alone will prove whether or not the actual disintegration of the organism by crushing is essential. By the method outlined, though the emulsion is free from clumps, the individual organisms for the most part remain intact.

Organism.	Media.	Age of culture: hours.	Devitalizing temp. one hour.	Dosage: millions.
Staphylococcus	Plain agar	12 to 18	60° C.	100 to 500
Streptococcus	Plain agar	24	58° C.	10 to 20
Pneumococcus	Serum	24	58° C.	50 to 100
Bacillus coli communis	Plain agar	8	54° C.	50 to 100
Bacillus pyocyaneus	Plain agar	12	54° C.	50 to 100
Gonococcus	Hydrocele-agar	6	60° C.	10 to 20
Meningococcus	Blood agar	18	60° C.	10 to 20

CASE I.—*Tuberculous ulceration of the bladder. Healed.*

P. N., aged thirty-four years, a mill manager and timber cruiser, was admitted to the service of Dr. Francis J. Shepherd, October, 1906, giving the following history: (1) Swelling, pain, and tenderness in the left testicle in 1898, subsiding after four months. (2) Hemorrhages from the bladder—the first in 1904; a second in May, 1906, associated with a moderate amount of pain and frequency of micturition; a third in July, 1906; and a fourth, one week before admission. (3) With the last hemorrhage pain and frequency of micturition became much more aggravated, necessitating the evacuation of the bladder every hour or hour and a half.

The patient is a robust-looking individual, weather-beaten and ruddy. External examination is negative apart from the presence of a quiescent nodule in the left globus minor.

On November 5 a cystoscopic examination by Dr. R. P. Campbell revealed the following condition: "The mucous membrane of the base of the bladder is congested and œdematous. On the left side posterior to the trigone is a yellow adherent mass of pus 5 mm. in diameter, covering the base of an ulcer. The right ureter only was catheterized, and after washing the bladder the urine from the left kidney was simultaneously collected, as it was secreted into the bladder, by means of an ordinary catheter. The examination of the common urine taken by catheter immediately before instrumentation and the separate urines obtained in the above manner resulted as follows:

Common.	Right.	Left.
Turbid	Clear	Turbid.
1025	1027	1025.
Acid	Acid	Acid.
Albumin present	No albumin	No albumin.
Urea 2.5 per cent.	2.6 per cent.	2.3 per cent.
Pus in quantity	None	A few pus cells, possibly from bladder contamination.
Tubercle bacilli present	Ureteral epithelium, no tubercle bacilli	Tubercle bacilli present, probably from the same source as pus cells.

The first inoculation of T. R. tuberculin $\frac{1}{1000}$ milligram was given November 5. The opsonic index to the tubercle bacillus was normal.

The patient was discharged from the hospital on the understanding that he should return every ten days for treatment.

November 13. Opsonic index, 1.25. Patient reports frequency of micturition slightly less troublesome, especially during the night. The chief improvement, however, has been in the marked decrease in the pain. No further hemorrhage. Gain in weight two pounds. Tubercle bacilli in large number were again found in the urine voided. In the preparation of the slides 30 per cent. nitric acid was used as a decolorizing agent.

November 22. Opsonic index, 1.25. The patient continues to progress favorably. The bladder is generally evacuated every three hours. The time, however, is variable. The pain is distinctly less and the patient is able to walk without experiencing the discomfort from which he suffered at the time of admission. There has been a further gain in weight of two pounds. Inoculation, $\frac{1}{1000}$ milligram.

December 1. Opsonic index, 1.2. Progressing favorably.

December 11. Opsonic index, 1.18. Gain in weight since commencement of treatment eight pounds. The patient is now able to retain urine for four hours. The pain is variable, but distinctly less than at the time of last inoculation. Inoculation, $\frac{1}{800}$ milligram.

December 21. Opsonic index, 1.18. The patient continues to do well. No further bleeding; no discomfort in walking; a further gain in weight of two pounds—that is, ten pounds since the first inoculation on November 5. Inoculation, $\frac{1}{1000}$ milligram.

January 4. Opsonic index, 1.1. Total gain in weight twelve pounds. Bladder symptoms as before. Inoculation, $\frac{1}{1000}$ milligram.

January 15. Opsonic index, 0.88. Since last inoculation the patient has been confined to bed for several days with an attack of influenza. The bladder symptoms during this period were distinctly aggravated. This illness may account for the sudden decline in the index and undoubtedly is responsible for a loss of four pounds in weight. Inoculation, $\frac{1}{800}$ milligram.

January 25. Opsonic index, 1.35. The patient has noticed a marked improvement in his condition since last reporting. Net gain in weight fourteen pounds, that is, an increase of six pounds in ten days. Inoculation, $\frac{1}{800}$ milligram.

February 8. Since last reporting January 25, the patient has been perfectly well and proffers the information that the nodules in the left globus minor have diminished considerably in size, which observation is confirmed by examination. Total gain in weight eighteen pounds. Opsonic index, 1.25. Inoculation, $\frac{1}{800}$ milligram.

The bladder holds 300 c.c. of fluid without discomfort, and a second cystoscopic examination by Dr. R. P. Campbell shows the

mucous membrane to be healthy throughout, with the exception of an area of œdematous swelling toward the left of the trigone and of some irregular ridges from among which the urine from the left ureter can be seen issuing. Save for this œdema and irregularity in the floor of the bladder there is nothing abnormal. No evidence is found of the former ulceration. The cystitis is confined to the œdematous area.

Comment. In the latter part of December tubercle bacilli were again found in the voided urine. The washed precipitate from a centrifugalized specimen was injected subcutaneously into a guinea-pig. Three weeks later the guinea-pig was killed, and caseous material from the glands of the groin transferred to a modification of Dorset egg medium (Duval). After five days the medium was found to be covered by a fine growth, the surface of the slants presenting the appearance of ground glass. Two tubes were opened and smears prepared, tubercle bacilli in pure culture being found. At the end of ten days transplants were made to bouillon flasks. It is our intention to prepare from the growth upon the latter a vaccine for use in the further treatment of this case.

This case has been selected from a series of three under observation. In all three improvement was marked after the first inoculation, pain being the first symptom to be relieved. In the first case of this series bilateral apical disease was associated with the infection of the urinary tract. In spite, however, of the wide distribution of the infection the patient has gained twenty pounds since the commencement of inoculations in August, 1906, with marked improvement in the urinary symptoms and pulmonary signs. The third case is of too recent date to be commented upon.

CASE II.—*Lupus vulgaris of the lip. Healed.*

W. G. G., aged twenty-nine years, medical student. About April, 1906, a tuberculous eruption appeared on the upper lip immediately below the margin of the left nostril, covering a skin area 1.5 cm. in diameter. This was treated locally with white precipitate ointment, resorcin, and other applications, all of which appeared to increase the irritation. After two months in the country some improvement was noted, but at the end of this period a large single tubercle appeared close to the original cluster. A small snipping from the original lesion was examined by Dr. Duval, who reported the condition to be tuberculous.

October 7. Opsonic index to the tubercle bacillus, 0.85. Inoculation of $\frac{1}{1500}$ milligram of T. R. tuberculin.

October 9. Opsonic index, 0.7. "Negative phase."

October 12. Opsonic index, 1.15. "Positive phase."

During October and November the eruption showed marked improvement. On February 1 the eruption upon the lip and margin of the nostril was apparently completely healed. There was a gain in weight since the commencement of the treatment of ten pounds.

Inoculations were given every ten days to two weeks, the dose since October having been $\frac{1}{800}$ milligram.

Comment. There can be no doubt as to the tuberculous nature of the eruption upon the lip, as the histological features were typical of tuberculosis and acid-fast bacilli were stained in the sections.

CASE III.—*Tuberculous arthritis and peri-arthritis of the wrist. Healed.*

M. M., aged twenty-five years. Pleurisy at eleven. Spinal caries at twelve—healed after five years' treatment. The family history is negative.

In 1901, following a slight injury, swelling of the left wrist with pain and loss of function were noted. This condition was operated upon some months later, with almost complete restoration of function. In May, 1905, the wrist again became painful and weak, loss of power in the extensors being the chief feature. The patient attended the Outdoor Department of one of the General Hospitals, where the wrist was enclosed at first in plaster-of-Paris and later in starch bandages. Subsequently she was treated by Bier's method, that is, from November, 1905, until admission to the service of Dr. Francis J. Shepherd at the Montreal General Hospital, July 18, 1906. At this time her condition was found to be unimproved.

On admission the left wrist was markedly swollen, painful, and tender, with prominence and posterior displacement of the head of the ulna and tenderness over the lower end of the radius. In front and behind the wrist-joint corresponding to the tendon areas were large pulpy swellings tender to pressure. Movements of the wrist-joint were very limited and painful. The muscles of the forearm and hand were atrophied and the fingers semiflexed at the terminal joints.

From the date of admission until August 11, Bier's bandage was applied daily without improvement. On the latter date the opsonic index to the tubercle bacillus was found to be 1.22.

The patient was given an inoculation of $\frac{1}{1500}$ milligram T. R. tuberculin. A small puncture was made with a scalpel over one of the tender points and a Klapp suction apparatus was applied for one hour, in periods of five minutes on and three off. At the same time a Bier's bandage was applied above the elbow.

This method of treatment led to almost immediate improvement and was continued until the patient was discharged December 8, 1906, four punctures in all having been made. When one puncture had so healed that the flow of serum almost or entirely ceased, a new puncture was made in another location where tenderness persisted.

The routine treatment consisted of (1) the adjustment daily of a Bier's bandage above the elbow half an hour before the application of the suction apparatus and its removal when aspiration was completed; (2) the application of the cup after swabbing the puncture

area with ether and lifting off the scab with the flat end of a probe; the amount of negative pressure employed was regulated by the degree of discoloration and the sensations of the patient, the desired result being a passive hyperemia without pain; and (3) the administration of T. R. tuberculin, $\frac{1}{1000}$ milligram every ten to fourteen days.

After the removal of the suction cup a small amount of boric powder was dusted over the puncture, and dry dressings were applied with a large pad of cotton-wool to prevent injury. The patient was at all times allowed to carry out movements unassociated with pain. In this way the nutrition of the muscles was improved and every advantage secured to the joints involved against increased fixation through contraction of adhesions.

At the end of four weeks a marked diminution had taken place in the inflammatory symptoms; partial although slight movement had been restored to the wrist-joint, and the fingers no longer remained semiflexed and rigid.

January 22. Since her discharge the patient has returned at intervals of ten days for inoculation. The condition at the present time is as follows: Complete absence of pain and tenderness in the left wrist-joint. The movements of the fingers are normal and in place of their former atrophied and pointed appearance they are now well rounded. There is very slight atrophy of the muscles of the hand. The movements of the wrist-joint remain markedly restricted, confined exclusively to flexion and extension. There is distinct improvement, however, in the nutrition of the extensor and flexor groups. The patient is able to lift light articles without discomfort. The general health of the patient is better than she has ever known. Since August there has been a gain of twelve pounds in weight.

Comment. The opsonic index to the tubercle bacillus was found, shortly after admission to be about normal, 1.15. This observation substantiates the theory held by us for some months that the result obtained by Bier in the treatment of tuberculous joints by hyperemia is due to the auto-inoculation thereby secured. This theory has recently been confirmed by the observations of Patch and Wells, carried out in Wright's laboratory, upon the blood of tuberculous patients treated by this method. These observers found that during the use of the bandage the blood, if taken at frequent intervals, showed recurring fluctuations in the immunity index varying in degree with the grade and duration of the Stauung (congestion). On removal of the bandage a more marked auto-inoculation was revealed by an increased negative dip and the development of a positive phase within twenty-four hours, the index rising to 1.30, 1.40, or higher. These observers were led to the conclusion that the use of a Bier bandage should be controlled by the opsonic index, as the dose, in an auto-inoculation from different joints and at different times from the same joint in the same individual, must necessarily vary. These conclusions furnish an explana-

tion of the frequent failures in the treatment of large joints by this method, and account for the untoward clinical phenomena following the prolonged daily use of the bandage above large joints. If such cases could be controlled by the index it would undoubtedly be found that not infrequently a "negative phase" had been engrafted upon a "negative phase" and in this way a gradual destruction of immunity units brought about. In the case reported the bandage was adjusted simply in order to secure an increased lymph tension in the diseased area, that is, an increase of lymph rich in opsonins. The use of the suction apparatus at this time not only removes stale, deopsonized serum, but promotes the inflow of more highly protective fluids into the diseased area. Further, the use of negative pressure at the time of the application of the bandage lessens the danger of superadding an auto-inoculation.

It is possible that Bier's method if controlled by the opsonic index furnishes an even more scientific method of treatment than the use of tuberculin, inasmuch as the material absorbed is the direct product of the particular strain of tubercle bacilli from which the individual is suffering, and theoretically more nearly approximates to what has been definitely established with regard to the use of vaccines prepared from staphylococci. On the other hand, the adjustment of the dose is a more difficult matter, and there remains finally the question whether the products of growth are as efficacious in arresting or retarding tuberculous disease as the actual bacterial protoplasm.

CASE IV.—*Tuberculous cervical adenitis. Improved.*

Miss A., aged twenty-four years. In 1901, two glands in the right posterior triangle of the neck became enlarged, underwent softening, and were incised. The sinus persisted for over a year. In 1903 several glands in the right axilla became similarly involved, were finally opened, and continued to discharge for three years. During the period 1900 to 1903 four other glands were noticed to be enlarged, that is, the pre-auriculars and two in front of the left sternomastoid. In the spring of 1906 the submaxillary glands became infected, together with several glands in front of the right sternomastoid.

The patient was admitted to the service of Dr. J. M. Elder, at the Montreal General Hospital, September, 1906. Examination showed the presence of a complete necklet of enlarged glands, varying in size, extending from below the right ear—beneath the chin—to a corresponding point on the opposite side, with discharging sinuses behind both angles of the mandible, in the submaxillary triangles, and in front of both ears—six or seven in all. In addition, enlarged glands were palpable in both posterior triangles and in the sublingual region. One especially large gland was noted in the anterior part of the right submaxillary triangle adherent to the lower border and inner surface of the jaw. There were also palpable

glands in the right axilla. The opsonic index to the tubercle bacillus was 0.82.

Owing to the extensive suppuration in the glands and tuberculous infiltration of the skin surrounding the sinuses, extirpation was considered inadvisable, and the patient was immediately placed upon inoculations of T. R. tuberculin every ten days. As Staphylococcus aureus had been secured in pure culture from the discharge the first three inoculations were combined with a vaccine of this organism containing 250,000,000 devitalized cocci to the dose. After the fourth inoculation all sinuses had completely closed and the patient showed a gain in weight of six pounds.

January 25. The patient continues to improve in general health. There has been a gain in weight of twelve pounds since commencement of treatment. All the outlying glands show a marked diminution in size. The large gland noted in the right submaxillary region is no longer tender, shows a marked decrease in size, and is quite movable.

Comment. In view of the history of prolonged suppuration associated with the earlier lesions the result obtained in this case is most striking from a clinical point of view. No doubt the prompt eradication of the associated staphylococcic infection favored an earlier inclusion of the tuberculous foci.

CASE V.—*Furunculosis. Cured.*

F., aged forty years, a foreman in the washroom of the hospital laundry, has been subject to succeeding crops of furuncles on the forearms, neck, and thighs for three months, during which time active lesions have always been present. On September 5 there were three acute furuncles on the anterior surface of the right forearm, one on the left forearm in the same location, one on the back of the neck, and one on the right leg. All were severe and in the acute stage. Cultures taken from one of the furuncles on the right arm yielded in eighteen hours a luxuriant growth of Staphylococcus aureus, from which a personal vaccine was prepared.

September 6. Opsonic index to staphylococcus, 0.62. Inoculation of 500,000,000 "personal" vaccine.

September 7. Opsonic index, 0.28. "Negative phase." The local signs are more severe.

September 9. A marked improvement is noted. The furuncles are much less painful and the surrounding blush has almost entirely disappeared.

September 10. Opsonic index, 1.72. There remain only small brown crusts the size of split peas, with slight underlying induration at the site of the lesions. None of the furuncles was incised or treated locally in any way.

January 25. The patient has remained absolutely free from further infections. A second inoculation was not considered necessary.

Comment. The foregoing represents the clinical type of staphylococcic infection which yields most readily to inoculation. From the organism isolated in this case the stock vaccine of Staphylococcus aureus was prepared, which was used in Cases VII and VIII, and in the primary inoculation in Case VI.

CASE VI.—*Carbuncle. Cured.*

F. M. D., aged fifty-five years, a clergyman. A man of robust physique, but overworked for the past two years. For three months previous to inoculation he suffered from a series of carbuncles, one lesion no sooner subsiding than another developed. The patient was first seen at the request of Dr. J. C. Cameron on December 14. Some days previous swelling and tenderness appeared at the base of the right middle finger—dorsal surface. The process gradually extended with the appearance of multiple foci of suppuration and tenderness in the axillary lymph nodes.

When seen December 14 a local septic infection existed at the base of the right middle finger with signs as above described. Owing to the patient's serious condition a 500,000,000 dose of staphylococcic vaccine was administered. A specimen taken from the finger for the determination of the opsonic index revealed a very pale, fluid condition of the blood; opsonic index to staphylococcus 0.58.

December 15. Agar slants from the carbuncle yielded pure cultures of Staphylococcus aureus.

When the patient was seen twenty-four hours after inoculation his general condition was found to be much improved. The axillary glands were free from tenderness. No further complaints of pain were made and the damaged finger could be handled without discomfort.

On December 17 the finger was quite normal apart from a moderate amount of induration and discoloration at the site of the lesion. Movements at the metacarpophalangeal and first interphalangeal joints were completely restored. Opsonic index, 1.28. The patient constantly reiterated his astonishment at the rapidity of his recovery.

On December 27 there were no signs of further suppuration. Opsonic index, 2. The patient, however, was given a second inoculation of 500,000,000 of "personal" vaccine as a precautionary measure.

February 1. The patient remains free from further infections.

CASE VII.—*Carbuncle. Cured.*

D. L., an Italian, aged fifty years, was first seen in the Outdoor Surgery December 7. Examination showed the presence of an area 10 x 10 cm. over the right scapula intensely inflamed and presenting numerous foci of suppuration. This area was also traversed by a crucial incision made two days previously. The discharge was profuse. In the interscapular area were numerous

furuncles in the acute stage. There was in addition an area of induration 10 cm. in diameter on the right side of the posterior surface of the neck embracing three distinct foci of suppuration, from one of which Staphylococcus aureus was isolated in pure culture. In order to save time, however, the patient was at once given an injection of 500,000,000 of "stock" vaccine.

The patient was not seen again for seven days, at the end of which time all signs of inflammation had disappeared from the lesions above described. There remained only a healthy granulating ulcer occupying the site of the crucial incision. Opsonic index, 1.22. Further inoculation was not deemed necessary.

CASE VIII.—*Suppurative periostitis. Cured.*

J. S., aged forty-five years, was seen in the Outdoor Department September, 1906. Examination showed a large fusiform swelling of the left middle finger with a sinus over the palmar surface of the middle phalanx. Denuded bone could be felt with a probe. The finger was extremely painful and tender. Gram positive cocci were found in smears. Opsonic index to staphylococcus, 0.75. An inoculation of 500,000,000 of Staphylococcus aureus vaccine was given.

Three days later the patient was again examined and the following condition noted: Marked diminution in the size of the finger. Complete absence of pain and tenderness. Complete absence of discharge. At the bottom of the sinus denuded bone could be seen. Although enjoined to report daily the patient failed to return for subsequent observation.

Later this patient was seen by Dr. Hillman, resident in charge of the Outdoor Surgery, who examined the finger and found it to be normal in appearance and function. The patient stated that he had not returned, as the sinus had healed rapidly without suppuration or separation of bone.

CASE IX.—*Multiple abscesses of the axilla. Cured.*

L. C., aged eighteen years, was admitted to the Montreal General Hospital, service of Dr. J. Alex. Hutchison, September 12, 1906. The patient was in good health prior to September 4. The first symptoms were stiffness and pain in the region of the right shoulder associated with chilly sensations. It was noticed that the shoulder was swollen and that a hard lump about the size of an egg could be felt in front of the joint.

On admission the patient was a well-nourished, anemic adult. A fluctuating inflammatory mass about the size of an egg was felt beneath the margin of the pectoralis major muscle. Cellulitis of the skin and subcutaneous tissue extended over the front and outer aspect of the shoulder and down the arm to the level of the insertion of the coracobrachialis muscle.

September 19. Incision of abscess with multiple incisions of the skin.

October 1. Wounds practically healed. About this time a number of pustules appeared in the vicinity of the cicatrix and also on the inner side of the arm. These were incised. One week later a hard mass appeared in the axilla about the size of a walnut. This was incised and pus evacuated.

During the following three weeks other abscesses continued to form in rapid succession in the superficial tissues of the axilla and were opened as they appeared, sometimes as many as two or there in a week. Owing to the serious impairment of the patient's general health and the progressive loss of function in the arm the patient was placed upon inoculations.

Agar slants from discharge yielded pure cultures of Staphylococcus aureus, from which a vaccine was prepared. First inoculation, November 22, of 500,000,000. Opsonic index to staphylococcus, 1.1.

October 26. Opsonic index, 1.5. A marked improvement is noted. The area of induration is very much lessened and all sinuses have healed.

October 29. Dressings discontinued as all signs of inflammation and suppuration have disappeared. There is complete restoration of the movements of the arm.

December 1. Opsonic index, 1.4. The patient still remains free from further suppuration.

January 8. The patient returned today complaining of a recurrence of tenderness in the axilla. Examination revealed the presence of a hard indurated mass the size of a filbert in the axilla near the posterior fold. Inoculation, 500,000,000. Arm bandaged without incision. Opsonic index, 0.70.

January 22. The patient has been seen several times since the last note was made and local examinations have always been negative.

February 1. The general health is greatly improved and the patient states that he has gained in weight twelve pounds.

Comment. This patient received in all five inoculations, although all symptoms disappeared after the first injection, with the exception of the slight disturbance observed on January 8, which it is interesting to note was coincident with a marked decline in the index.

CASE X.—*Acne indurata. Cured.*

S., aged twenty-three years, a medical student, has had acne indurata of the face for the past four years. He was seen first on October 10, 1906, at which time there were numerous active pustules present upon both cheeks, with extensive scarring. His general health was good. Various methods of treatment had been tried, but without even temporary improvement.

October 12. The patient was inoculated with 500,000,000 staphylococcus albus "personal." Opsonic index to staphylococcus normal.

October 22. A marked improvement is noted. No new pustules. Opsonic index, 1.7. A second inoculation of 500,000,000 was given.

Following this the patient had a severe negative phase with an increase in the local inflammatory signs which persisted for six or eight days and were followed by a second period of improvement.

December 10. No further pustules have developed. The skin of the cheeks has become much paler than at any time previously. Further inoculation was not considered necessary.

December 18. The patient still remained absolutely free from pustules and expressed great delight at the result achieved. A further inoculation of 250,000,000 was given as a precautionary measure.

February 1. There has been no further pustulation and the skin of the cheeks has become soft and pliable. The purplish discoloration in the scars has almost entirely disappeared except when exposed to cold.

Comment. Several cases of this affection have been under observation and the results obtained have varied directly with the duration of the disease. While long-standing cases (six to eight years) show marked improvement after the first inoculation it is necessary to continue the treatment over a much longer period of time; apparently the presence of the scar tissue with the attendant defects in the circulation plays an important role in delaying a cure. We have found a valuable adjunct in the management of such cases in the active hyperemia induced by the application of hot-water stupes for a period of twenty minutes daily. By this means the defects in the circulation are overcome. Further, it has been noted that after inoculation in old-standing cases the local signs are more prone to exacerbations, necessitating not infrequently a reduction in the dosage.

As the treatment of acne indurata is always more or less prolonged we have been able on several occasions to make observations upon the effect of inoculation on the viability of organisms in unopened pustules, and have repeatedly obtained during the positive phase pus from apparently active lesions which yielded negative results upon ordinary media.

Our experience with the use of stock vaccines in the treatment of such cases has been unsatisfactory, confirming in this respect the writings of Wright, Weinstein, and others upon the importance of preparing in each case a personal vaccine.

Without exception the organism isolated in these cases has been Staphylococcus epidermidis albus (Welch), yielding upon plain agar within twenty-four hours medium-sized china-white colonies of Gram-positive cocci.

CASE XI.—*Gonorrhœal polyarthritis. Cured.*

W. M., aged twenty-one years. Admitted to the Montreal General Hospital, service of Dr. Finley, December 10, 1906, with a history of urethral discharge dating from December 1, and complaining of severe pain and swelling in the right shoulder, left wrist,

and metacarpophalangeal joint of the left thumb. The joint symptoms manifested themselves simultaneously on December 6, in the three joints described; the pain and swelling reached their present degree of intensity within forty-eight hours.

Examination revealed the presence of: (1) A profuse urethral discharge, which on examination was found to contain numerous intracellular diplococci decolorized by Gram's stain. (2) An acute arthritis of the right shoulder, left wrist, and metacarpophalangeal joint of the left thumb.

From the date of admission until December 24, the joint lesions were treated locally with fomentations of lead and opium, without improvement. During this period the temperature ranged daily between 99.3° and 101.3° F.

December 25. The patient was given an inoculation of stock gonococcus vaccine—10,000,000. Opsonic index to gonococcus, 0.85

December 26. The patient states that he feels somewhat better. No improvement is noted in the joint condition.

December 27. Opsonic index, 3. A most striking change has taken place in the arthritic lesions; the patient freely moves the left hand and abducts the right arm to a right angle with the body with rapidity and ease. Temperature range, 98.1° to 99°. There is a very marked decrease in the urethral discharge.

From this date the joint symptoms rapidly abated, and when the patient left the hospital January 2 he was able to carry out the fullest movements in the shoulder and wrist-joints without pain.

On January 7 the patient resumed his occupation as typewriter.

A second inoculation of 10,000,000 was administered on January 4 and a third on January 14. On the latter date the urethral discharge had entirely ceased.

February 8. The patient has remained absolutely free both from articular and urethral symptoms.

Comment. Our attention was first drawn to this infection by the striking evidence of auto-inoculation uniformly manifested during the acute stage of gonorrhœal epididymo-orchitis in the sudden cessation of the urethral discharge. With the backward extension of the disease and the attendant inflammation there takes place an absorption of gonococcus toxins—in some cases of the organisms themselves—leading as we have found to a marked rise in the immunity index, which latter feature is responsible in our opinion for the marked decrease or complete disappearance of the urethral discharge; an attenuated discharge reappearing in the majority of cases with the decline of the complicating inflammation and the concurrent ebb of the immunity. The index seldom, however, falls below normal.

Prompted then by the results of auto-inoculation interpreted along the above lines, three patients with acute gonorrhœa, complicated by polyarticular inflammation, have been subjected to inoculations

of gonococcic vaccine. In all three the effect upon the urethral discharge was identical with the phenomena to be observed in epididymal involvement: the cessation of the discharge following the development of a strong positive phase. The following indices were recorded: Case I, forty-eight hours after inoculation, opsonic index, 1.6. Case II, forty-eight hours after inoculation, opsonic index, 2.8. Case III, twenty-four hours after inoculation, opsonic index, 3. The last is the case reported. Case I received a second inoculation and was discharged well. Case II was admitted from the Out-patient Department owing to extensive effusion into the knee-joints and remained under observation for four months owing to the persistence of the effusion in the right knee, leading eventually to partial fibrous ankylosis. Fluid aspirated from the right knee on two occasions was sterile and no organisms were found in smears.

CASE XII.—*Epidemic cerebrospinal meningitis. Recovery.*

L. B., aged twenty-eight years. Admitted to the Montreal General Hospital December 21, service of Dr. F. G. Finley, complaining of severe pain in the back of the head, supra-orbital regions, and the small of the back, and also of chilly sensations alternating with profuse sweats.

The patient was in good health until December 17, when he contracted what he describes as a severe cold, and felt "all choked up in the head." From December 18 to the time of admission pain in the head had been constant. There were sharp pains in the occipital region radiating forward to the supra-orbital regions. Additional symptoms were chilly sensations, frequent sweats, and occasional vomiting.

On admission he was well nourished; the skin was hot and dry; mucous membranes were of good color. The patient felt chilly and suffered from severe paroxysms of pain in the back of the head which caused him to cry out and groan. The tongue was coated. The bowels were constipated. The abdomen was normal. The urine was clear, acid, 1041, no albumin, 1.54 per cent. sugar. Microscopically, a few pus cells and mucous threads.

The mind was clear. There was no retraction of the neck, but the patient was unable to approximate the chin to the sternum and any attempt to pull the head forward caused great pain. Kernig's sign was present on both sides, and there were slight fibrillary twitchings in the left calf muscles. The plantar reflexes and the knee-jerks were increased. Achilles, cremasteric, abdominal, epigastric and supra-orbital reflexes were marked.

December 22. Temperature rose from 99° at noon, to 103.6° at 4 P.M., with general symptoms as before noted. At 12 M. lumbar puncture was performed and 1.5 c.c. of turbid fluid withdrawn, containing numerous polynuclear neutrophilic cells. A few intracellular diplococci decolorizing by Gram were found. At 6 P.M. the patient was given hypodermically an injection of meningococcic

vaccine containing 15,000,000 devitalized organisms. The patient's opsonic index to the meningococcus taken at the same time was found to be approximately normal.

December 23. Temperature range 101° to 102°. The headache has been less intense. There is profuse sweating at irregular intervals. Cultures from the spinal fluid upon blood agar show at the end of twenty-four hours numerous colonies of meningococci.

December 24. Opsonic index, 1.5. Temeprature range, 100° to 102°. The headache continues, but is less severe. There is constant ache with pain on pressure in the muscles of the lumbar region. Kernig's sign is still present, but the angle of extension is greater, 135° on both sides. Sugar in the urine, 0.48 per cent.

Examination of the eyes by Dr. George M. Mathewson shows "optic neuritis in both eyes—distinct but of moderate degree. No hemorrhages or white masses in the retinæ."

December 27. The patient complains only of a slight pain in the back. The right pupil is dilated, the left slightly contracted; both react to light. Reflexes normal. The patient is able to bring the chin close to the sternum without much pain. Kernig's sign is still present. Temperature range 98° at 8 A.M. to 100° at 4 P.M. General condition much improved. Sugar—a trace only.

January 1. Kernig's sign is absent; all reflexes are normal. The right pupil is still a little larger than the left. No pain in the back or head. The patient is feeling much better in every way. No sugar.

January 3. Opsonic index, 5.9. The patient feels and looks well. Temperature range for the last twenty-four hours, 97.4° to 99.4°. No headache or pain in the back. Very little rigidity of the muscles of the neck. Reflexes normal, pupils equal and active. Further inoculation not considered necessary.

Comment. Attention is directed to the following points in connection with this case: (1) It is scarcely probable that the small amount of fluid removed (1.5 c.c.) could have influenced the course of the disease. Temporary improvement is undoubtedly seen after spinal puncture, generally when larger quantities than the above are removed. In the present instance further puncture, though under consideration, was postponed from day to day owing to the patient's steady progress toward recovery. (2) Glycosuria was found as a rare concomitant and it is interesting to note that with the rise in the index the glycosuria rapidly disappeared. (3) Exacerbations so frequently observed in the cases of moderate intensity were not noted in the present instance. (4) An extremely high immunity index was noted on January 3. In view of the results obtained by Flexner in his experimental work upon the protective powers of the serum of immunized monkeys this was not unexpected, and in our opinion was due directly to the immunity induced by inoculation, as observations made in June, 1906, upon the serum of a patient con-

valescent from subacute epidemic cerebrospinal meningitis yielded indices below the normal.

CASE XIII.—*Epidemic cerebrospinal meningitis. Recovery.*

A. M., aged seven months. Admitted to the service of Dr. F. G. Finley, at the Montreal General Hospital January 28, 1907. The present illness began January 15, with fever, pain referred to the neck, and retraction of the head. The temperature rose rapidly to 105° and subsequently ranged between 100° and 104° until admission. Neither vomiting nor convulsions occurred. Bowels constipated. On admission the patient was a well-nourished Hebrew child. He lies upon the side with legs and thighs flexed. The head is retracted and rotated to the right and attempts at manipulation cause great distress. Temperature at 2 P.M., 104.2°.

Shortly after admission lumbar puncture was performed and 45 c.c. of turbid fluid withdrawn. Cover-slip preparations showed numerous meningococci, both free and intracellular. Cultures were positive at the end of twenty-four hours. The opsonic index to meningococcus was 0.68. Inoculation of meningococcic vaccine, 7,500,000.

January 31. Opsonic index, 1.8. Temperature range, 99.2° to 103°. The child is steadily improving.

February 5. Opsonic index, 1.58. Temperature range, 100° to 102°. Inoculation, 7,500,000. The child continues to progress satisfactorily.

February 6. Temperature range, 100° to 100.6°. The child is much better in every way.

February 8. Opsonic index, 1.2. From this date until February 11 the temperature ranged between 98.2° and 99.1°. On February 11 the temperature rose from 99° at 8 P.M. to 102° on the morning of February 12, with return of cardinal symptoms. Inoculation, 7,500,000.

February 13. Temperature range, 97.4° to 98.1°. The child is apparently convalescent.

February 15. Opsonic index, 2.8. A final inoculation of 15,000,000 was given. From this date convalescence was uninterrupted.

Comment. In this case the notes have been drawn to accentuate the effect of inoculation upon the temperature range. The second lumbar puncture was performed on January 31, as a result of the index finding, in the hope that the removal of deopsonized fluid would favor the inflow of a lymph approximating in opsonic power the individual's blood serum. When large quantities of fluid are removed by lumbar puncture the part played by the replacing lymph must come to be considered in the light of an auto-inoculation. It is our opinion that in the management of these cases lumbar puncture should be practised at frequent intervals in order to rid the spinal lymph space of fluid incapable either of destroying or inhibiting the growth of the infective agent. That the cerebrospinal fluid with-

drawn in such cases has been reduced in opsonic power is shown by the fact that incubation increases very considerably the number of diplococci present. Upon this important point we are at present at work and hope shortly to publish our results in full.

CASE XIV.—*Epidemic cerebrospinal meningitis. Death. Autopsy.*

H. G., aged forty years, a jeweller. Admitted to the service of Dr. Molson, at the Montreal General Hospital, February 28, 1907.

The present illness began February 13, with severe chill, intense headache, and stiffness of the neck developing within twenty-four hours. Vomited once.

February 16. The patient no longer recognized his family, remaining in this semiconscious state until admission.

On admission the patient responds to repeated requests to turn in bed or protrude the tongue, but is unable to speak. The face is expressionless. Movements of the head cause intense pain. Kernig's sign is marked. The temperature is subnormal.

March 1. Lumbar puncture was performed and 15 c.c. of turbid fluid was withdrawn, containing numerous meningococci, both free and intracellular. (Twenty-four-hour cultures positive.) Inoculation of meningococcus vaccine, 15,000,000.

March 3. Condition unchanged. Muttering delirium is noted at times, with frequent picking at the bed-clothes. Temperature at 12 M., 102°.

March 6. The patient is quite unconscious and cannot be aroused. Temperature, 98.2°; pulse, 60. Inoculation, 30,000,000.

March 7. Condition unchanged. Temperature, 97.4°.

March 8. Inoculation, 30,000,000. Lumbar puncture performed and 10 c.c. of fluid withdrawn, containing meningococci as before. (Twenty-four-hour cultures positive.)

March 9. The patient's mental state today shows a marked improvement. He answers questions rationally, looks bright, and is able to take feeder from attendant. Rigidity of the neck and extremities is still marked. Temperature, 100°.

March 10. The patient's mental condition continues to improve.

March 11. It is difficult to arouse the patient this morning; nourishment is not so well taken and the expression is again lethargic. At 12 M. the patient became cyanosed, and died at 3 P.M.

Extract from autopsy protocol. Thirty-six hours after death (Dr. Duval). The longitudinal sinus contains fluid blood. On stripping back the dura the brain substance is quite dry and the convolutions markedly flattened. Pial vessels are deeply injected. At the base of the brain in the region of the pons there is considerable opacity of the meninges, while in places there is a dry, plastic exudate. Brain weight, 1200 grams. The lateral ventricles are greatly dilated and filled with slightly turbid fluid in which there is some fibrin. The Sylvian canal is plugged with this fibrinous material. The

fourth ventricle appears normal. The pons, medulla, midbrain and basal ganglia show nothing remarkable. The hemispheres, the optic thalami, and the striate bodies are more or less œdematous. In the cover-slip preparations from the exudate in the pontine region and from the ventricular fluid no diplococci were found. Cultures negative.

Comment. We would draw attention to the fact that while viable diplococci were present in the fluid withdrawn from the spinal canal three days before death the autopsy findings showed a complete arrest of the meningitis. Unfortunately the lapsed time between death and the postmortem examination detracts greatly from the value of the bacteriological observations.

While we do not presume to draw conclusions from the treatment of so few cases we certainly look forward to the acquisition of additional evidence upon the value of bacterial inoculation in this affection, both in the field of protection and of cure.

General Conclusions. Our observations confirm in general the dictum of Wright that an individual suffering from a localized infection has a low opsonic index to that particular infection. We have found low indices to be the rule in afebrile tuberculous lesions, in furunculosis, and in acne during the earlier stages. Long-standing cases of acne have been found in our experience to yield indices between 0.90 and 1.1. In this connection the uniformly low indices noted by Weinstein are remarkable.

When the lesions are exposed to view, as in lupus, furunculosis, and acne, the first effect to be noted is a rapid subsidence of the inflammatory signs, which explains the early diminution in the subjective symptom of pain in such deep-seated lesions as tuberculous ulceration of the bladder, tuberculous arthritis, and meningitis. This relative anemia is invariably associated with the development of a positive phase just as increased congestion is, in the majority of cases, the concomitant of a negative phase.

While the opsonic index is a most valuable guide in regulating the amount and time of dosage, we are of the opinion that excellent results may be obtained, especially in the treatment of localized tuberculous lesions, without the use of the "Immunity Thermometer;" success in the vast majority of cases attending the employment of minute doses at long intervals, the dose beginning preferably with $\frac{1}{1500}$ milligram to be gradually increased to $\frac{1}{800}$ milligram, providing always that increases are unattended by constitutional symptoms. Generally speaking the feelings of the patient are a safe guide. Trudeau persisted in the use of tuberculin throughout the period when tuberculin was least in favor, and with most encouraging results, the guiding principles in his use of it being minimal dosage and wide spacing.

In our experience "an accumulation in the direction of a positive phase" is not to be looked for in the treatment of tuberculous cases.

The same remark applies to staphylococcic infections. Generally speaking the most that can be hoped for in these infections is a maximum in the direction of a positive phase and a minimum in the direction of a negative phase. On the contrary, in such infections as gonorrhœa and epidemic cerebrospinal meningitis high indices may be produced by inoculation, and from the striking effects of inoculation observed in gonorrhœa and the analogy which exists between the two infections, we are emboldened to hope that in bacterial inoculation may be found the form of therapeutics destined to combat effectively meningococcal infections.

TECHNIQUE. No pains have been spared to make the technique in connection with the determination of the indices as perfect as possible. Sera are collected at the same hour each day and the controls taken at the same time. Washed corpuscles are always prepared immediately before use, as we have found that in those which have stood for some time many of the polynuclear neutrophiles fail to functionate. In counting we determine the content of one hundred cells, and in the case of tubercle prepare slides from two control sera, the average being taken as the normal standard. In this determination the counts have on some occasions been exactly similar—the variation as a rule not exceeding the average per cell.

We prepare our tubercle suspension daily by rubbing up in an agate mortar a small portion of an emulsion of tubercle bacilli with 1.5 per cent. NaCl solution, centrifugating, and drawing off and thoroughly mixing the supernatant fluid. The strength of the suspension thus obtained is determined by putting through a "trial trip" with control serum and subsequently diluting the suspension so that the cell average may not exceed 4 to 6. Suspensions thus prepared and standardized rapidly deteriorate through clumping, and for this reason we are forced to the laborious undertaking of preparing daily a fresh suspension.

In preparing suspensions of other organisms 0.85 per cent. NaCl solution is employed, young cultures are used, and the density is determined by the naked-eye appearance.

In conclusion we wish to express our gratitude to Dr. Duval, Director of the Laboratory of the Montreal General Hospital, for his very special assistance and advice in connection with the bacteriological side of our work. Our thanks are also due to the members of the attending staff who have placed material at our disposal, and to Sir Almroth E. Wright for the opportunities enjoyed in his laboratory at St. Mary's Hospital, and for his encouragement of our efforts during his recent visit to Montreal.

THE OPSONIC INDEX IN DIABETES MELLITUS.[1]

A PRELIMINARY RECORD OF THE FINDINGS IN 22 CASES OF GLYCOSURIA, WITH REMARKS ON THE TECHNIQUE OF THE OPSONIN TEST AND ON ITS CLINICAL UTILITY.

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The objects of this paper are twofold: (1) To present a preliminary record of the behavior of the opsonic index in diabetes mellitus; and (2) to draw attention to certain errors and technical difficulties in opsonin testing—drawbacks which may keenly discourage the beginner, and even in the experienced worker at times arouse skepticism about the real value of the test. The experiments herewith reported were made, with the help of my co-worker, Dr. E. J. G. Beardsley, in the clinical laboratory of the Jefferson Medical College Hospital.

In selecting diabetes mellitus as a disease not unlikely to show deviations from the normal opsonic values, we were influenced primarily by the undue susceptibility of many diabetics toward bacterial infections, notably of the cutaneous and pulmonary systems —a tendency perhaps to be explained by a low opsonic content in the blood plasma of the person thus affected. Furthermore, the grave metabolic disturbances of diabetes, leading, for example, to hyperglycemia, to lipemia, and to the accumulation of β-oxybutyric acid in the blood and other tissues, prompted, on *a priori* grounds, the query, "How much, if at all, do these changes influence the blood opsonins?"

THE OPSONIC INDEX IN GLYCOSURIA.

Of the 22 patients studied, 16 were examples of diabetes mellitus, 4 of diabetes insipidus, and 2 of transient, "accidental" glycosuria. Staphylococcus pyogenes aureus was chosen as the bacterium with which to determine opsonin values in all the tests, since it is to infections from this source that the diabetic appears to be highly vulnerable. The following data, therefore, relate to the opsonic indices toward the staphylococcus alone.

Of the cases of true diabetes mellitus, all had subnormal opsonin indices, ranging between 0.34 and 0.72, and averaging 0.62 for the

[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, March 11, 1907.

series of 16 patients. The individual figures for these cases were, consecutively, as follows: 0.66, 0.44, 0.68, 0.49, 0.52, 0.67, 0.59, 0.59, 0.60, 0.34, 0.72, 0.46, 0.67, 0.62, 0.46, and 0.49. On analysis of the histories of the foregoing cases, it was found that 3 in which the urine gave positive tests for acetone and diacetic acid showed especially low opsonin values: 0.49, 0.52, and 0.34 in Cases IV, V, and X, respectively. These findings, though suggestive, should not, on such meagre data, be interpreted as indicating that acidosis especially lowers the opsonic index; on the contrary, extremely subnormal values may occur in the absence of these urinary changes, as in Cases II (index, 0.44), XII (index, 0.46), XV (index, 0.46), and XVI (index, 0.49), in none of which was acetone or diacetic acid detected. In the cases thus far studied no relationship between the sugar content of the urine and the opsonic value of the blood could be determined in the individual instance, low opsonic figures having been met with in patients with moderate glycosuria, and *vice versa*. Albuminuria seemed also to have no effect upon the subject's opsonicity. No relationship could be established between the leukocyte count and the opsonic content of the serum, and the same was true of the hemoglobin and the erythrocyte figures. This bare statement will be substantiated when sufficient data have been collected to justify a more detailed discussion of the subject. Here may be noted, however, Bulloch and Ledingham's experiments[2] which showed that the injection of tallianin, though it promptly excites leukocyte increase, fails to raise the opsonic index; while in many of the patients to whom Huggard and Morland[3] administered yeast, in their studies of its effect in tuberculosis, subnormal leukocyte counts were found to be compatible with high opsonin figures and the reverse of this was likewise true.

For the 4 cases of diabetes insipidus examined, indices of 0.82, 0.82, 0.87, and 0.89 were calculated, these figures being within the normal range, which varies between 0.8 and 1.2, according to Bulloch's studies of 84 healthy subjects.[4] The average index of these cases (0.85) is a decided contrast to that of diabetes mellitus (0.62), though it is of course obvious that the former is based upon too small a number of tests to be comparable with the latter. It may also be noted that the indices found in diabetes insipidus, though individually within the range of health, collectively average some ten points below the average normal figure, which is generally conceded to be 0.95.

Of the 2 patients with transient glycosuria, 1 showed an index of 0.81 and the other an index of 0.91; the former was an example of postoperative glycosuria, while in the latter the patient's temporary glycosuria was traced to overindulgence in malt liquors.

In view of the numerous and convincing studies of opsonins

[2] Lancet, 1905, ii, 1603.
[3] Lancet, 1905, i, 1493.
[4] Trans. Path. Soc. Lond., 1905, lvi, 334.

made during the last year or two, it need hardly be explained that the presence of these substances in the blood serum is essential to the display of phagocytosis by the cells concerned in this defensive process against disease due to bacterial invasion of the human organism. This impotence on the part of the leukocytes to engulf microörganisms, unaided by the opsonic substances of the blood, has been decisively proved by Wright,[5] Douglas, Bulloch,[6] and others, who have shown that after the incubation of equal units of a bacterial emulsion, washed leukocytes, and blood serum which has been heated to 60° C., the leukocytes of the mixture contain no bacteria whatever; on the other hand, if unheated serum be employed in a precisely similar test, the leukocytes are found to be crowded with bacteria which these cells have engulfed and are digesting. The inference from such an experiment is that the failure of the cells to act as phagocytes in the first instance and their ability to do so in the second, is referable to the influence of opsonic bodies, which are thermolabile, and to all intents and purposes disappear from the blood serum after it has been heated for a short time at a temperature of 60° C. It is believed that the opsonins combine with the invading bacteria and in some manner cripple them so as to favor their ingestion by the phagocytic leukocytes, which, without this preparatory attack by the opsonins, are incapable of becoming bacterial destroyers. Thus, while opsonins do not directly stimulate the leukocytes to exert bactericidal properties, they bring about such an action by their effect upon the offending microörganisms. The opsonic index of a given blood may be regarded as the capacity of its serum to stimulate phagocytosis, for the higher the opsonic content of the serum the more active the power of its leukocytes to engulf bacteria. In passing, it is of interest to mention the prevalent belief, that the blood serum contains different opsonic substances, each of which has selective combining properties with certain bacteria—an adequate opsonic index toward the staphylococcus does not mean an equal power of repelling invasion by the streptococcus, the pneumococcus, or the gonococcus. That the specificity of opsonins is more than a convenient hypothesis seems true, from the behavior of these substances in an advanced case of pulmonary tuberculosis, in which, despite the grave inroads of the infection, the patient's blood may show a high index toward the tubercle bacillus and a low index toward the streptococcus. This suggests not only a multiplicity of opsonins, but also indicates an adequate acquired resistance toward Koch's microörganism linked with a feeble opposition toward the streptococcus, to the secondary invasion of which most of the late severe symptoms of phthisis are referable.

This inquiry establishes merely the fact that diabetics show

[5] Proc. Roy. Soc., vol. lxxii, p. 357. [6] Loc. cit.

feeble resistance toward staphylococcic infections, if one may gauge this property by the behavior of the opsonic index toward the specific bacterium of such processes. If this be true, it may explain the prevalence of boils, carbuncles, abscesses and similar lesions in this disease, but it is premature to assert that all subjects thus affected show especially wide deviations from the normal standard, despite the apparent obviousness of this relationship in an occasional instance. The existence of a high opsonic figure in a subject of furunculosis suggests that the individual's resisting powers are being vigorously exerted. The opsonic activity of diabetic blood toward the streptococcus, the tubercle bacillus, and other microörganisms remains to be investigated, and these studies will be the subject matter of a subsequent report.

Theoretically, it is convenient to assume that the subnormal opsonic values in diabetes are due to an inherent deficiency of opsonins, or to the antagonistic action of anti-opsonins. The latter substances neutralize the activity of opsonins without injuring the leukocytes, as shown by the experiments of Hektoen and Reudiger[7] on the anti-opsonic action of calcium chloride, barium chloride, lactic acid, and other substances. May not antiphagocytic bodies of this sort arise in consequence of the metabolic disturbances so intimately a part of the diabetic state? It may be that further investigation will establish some relationship between the opsonic content of the blood plasma and the hormon bodies, of which the substance "secretin" apparently is a real factor of certain forms of diabetes. If the admirable studies of Bayliss and Starling[8] be accepted, secretion is produced by the action of dilute acids (*i. e.*, acid chyme) on the duodenal mucosa, whence it is carried by the vessels to the pancreas upon which it acts as a stimulant to the secretion of pancreatic juice. It has also been suggested that secretin has the same effect on the internal secretion of the pancreas, and if this be true, its influence on glycosuria is obvious, granted, of course, that the pancreas is not too extensively diseased to respond to stimulation. In this connection may be noted Bainbridge and Beddard's report[9] on the finding, in 5 of 6 cases of diabetes without pancreatic lesions, minimal quantities of secretin in comparison with the amount of this material discovered in subjects dead of non-diabetic diseases.

OPSONIN TECHNIQUE.

It is obvious to anyone who has worked with the opsonin test that satisfactory results demand considerable patience, a certain manual dexterity, and an absolutely faultless technique on the part of the

[7] Jour. Infect. Dis., 1905, ii, 129 and 141.
[8] Jour. Amer. Med. Assoc., 1907, xlviii, 524.
[9] Biochem. Jour., 1906, i, 429.

examiner, for the lack of which one's theoretical conception of the subject, however thorough, and the laboratory equipment at one's command, however elaborate, can never compensate. On paper, the test is a simple procedure; but in the laboratory it necessitates most rigid adherence to each technical detail, from the collection of the blood sample until the stained specimens are placed on the stage of the microscope. One false step may be sufficient to negative the result of an hour or two of continuous work. Briefly, the opsonic power of any given blood is ascertained by comparing the phagocytic activity of its serum with that of a normal serum used as a control, the resulting figure being known as the "opsonic index" of the blood in question. This is accomplished by mixing in a pipette equal parts of a bacterial emulsion, washed leukocytes, and the serum to be tested; incubating this mixture for a definite period at body temperature; and, finally, counting the bacteria ingested by a certain number of the leukocytes. Two tests are made in this

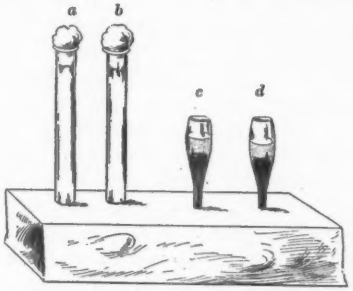

FIG. 1.—Test tube rack: *a*, bacterial emulsion; *b*, washed leukocytes; *c*, serum to be tested; *d*, control serum.

FIG. 2.—Wright's tube.

FIG. 3.—Test tube.

manner: one with the patient's serum and the other with the serum of a healthy person, to serve as a control, the same bacterial emulsion and washed leukocytes being, of course, employed for both.

The details of this process, with its common sources of error, may be conveniently described under these headings:

I. Collecting the blood and separating the serum.
II. Preparing the bacterial emulsion.
III. Obtaining the washed leukocytes.
IV. Measuring, mixing, and incubating the units.
V. Preparing and examining the stained films.

SPECIAL APPARATUS The special apparatus required for opsonin work comprises collecting tubes, test tubes for the washed leukocytes and for the bacterial emulsion, capillary mixing pipettes, and ordinary suction pipettes. A wooden rack (Fig. 1) for holding the several liquids will prove most advantageous in the procedure of measuring the units. Wright's tubes (Fig. 2) are by far the most

satisfactory device for collecting the patient's and the control bloods. They are fashioned of glass tubing, which is drawn out at one end into a straight point not more than 1 mm. in diameter, while the other extremity is bent in the form of a *J*, the caliber of which should be of capillary fineness. The length of such a tube, from bend to straight end, is 6 cm., its greatest diameter is 5 mm., and its capacity is 1 c.c. Test tubes (Fig. 3), used in obtaining the washed leukocytes, hold 4 c.c., have a length of 7 cm., and a diameter of 9 mm.; the latter measurement is important, for it is difficult to fill a smaller-sized tube, and with a larger caliber the zone of leukocytes thrown down by centrifugalization is so shallow that it can be pipetted off only with great difficulty and much uncertainty. Tubes of the same dimensions are of a convenient size for containing the bacterial emulsion. The mixing pipettes (Fig. 4) are made of 5 mm. tubing, preferable with a relatively thick (0.5 mm.) wall, in order to avoid undue breakage. One end is drawn out into a very fine bore 15 cm. in length, and to the other end is fitted a soft rubber nipple, which may be attached directly to the larger end of the pipette, or coupled to it by a throttle and two short lengths of rubber tubing, if it be considered advisable to ensure better control of the columns of liquid while measuring the units of bacteria, leukocytes, and serum. A throttle suggested by Wright (Fig. 5) consists of an outer glass shell 5 mm. in diameter at each end, and constricted in the middle where it encloses a fine needle-like capillary tube, held in place by sealing wax, with the pointed end toward the nipple. A device of this sort has been applied by Boggs[10] to the hemocytometer, and its use in opsonin estimations is of distinct service, should one have difficulty in measuring accurately the units with the aid of a plain nipple. In lieu of such a device, a plug of cotton may be thrust into the pipette between the expansion and the "nipple end," to control the suction force. A handy form of suction pipette (Fig. 6) for removing the liquid from the washed leukocytes may be of a bit of 5 mm. tubing, about 15 cm. long and provided with a central extension 10 or 12 mm. in diameter; a similar tube is also helpful in removing the bacterial emulsion after centrifugalization. These pipettes, it may be added, are not absolutely essential, for ordinary large medicine droppers may be used instead. A few glass watch crystals, covers, and slides comprise the other glassware used in the tests. Experience has taught that for rapid and accurate work a high-speed electric centrifuge is indispensable for obtaining the washed leukocytes and for separating the serum from the whole blood without delay. In the Jefferson Clinical Laboratory, we use a centrifuge revolving 8000 times a minute, driven by a $\frac{1}{12}$ horse-power motor supplied by a 110-volt direct street current. Water-power centrifuges, which give at the most

[10] Jour. Amer. Med. Assoc., 1907, vol. xlviii, p. 49.

but 1000 or 1200 revolutions a minute, have not proved satisfactory in our hands.

I. *Collecting the Blood and Separating the Serum.* This is a simple procedure if a properly blown Wright's tube is used in the manner herewith illustrated (Fig. 7). Failure to obtain a steady flow of blood into the body of the tube may be due to deficient and intermittent bleeding from the puncture, or to an improperly con-

Fig. 4.—Mixing pipette.

Fig. 5.—Wright's throttle.

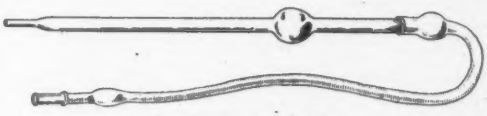

Fig. 6.—Suction pipette.

Fig. 7.—Method of collecting the blood with Wright's tube.

Fig. 8.—Serum and clot after centrifugalization.

structed tube. The first source of trouble is removable by making a puncture sufficiently large and deep to ensure a rapid, continuous movement of the blood column through the tube's capillarity, the end of which must be kept immersed in the blood until the tube is sufficiently filled, that is, to about two-thirds its capacity. In consequence of these precautions the capillarity does not become blocked by partly formed clots, as is the case when the blood oozes from the wound in single drops, the collection of which halts the onward movement of the blood as the tube is applied to each drop, thereby favoring more or less drying, coagulation, and interruption

of the column. The flow of the latter is materially hastened by gently heating the straight portion of the tube just before use. The employment of tubes conforming to the dimensions given above will eliminate perplexities referable to faulty apparatus. After collecting the blood the extremity of the straight portion of the tube is sealed in a flame and allowed to cool, after which it is grasped by its curved arm and shaken, as one shakes down the mercury column of a clinical thermometer, in order to drive the blood into the body and the tapering end. The tip of the curved arm is then sealed, to prevent evaporation, and the tube placed, straight end downward, in the centrifuge shield and centrifugalized, to separate the clot and the serum (Fig. 8). The latter is removed with a pipette at the time of the test, the wall of the tube having been scored with a file and broken.

II. *Preparing the Bacterial Emulsion.* About 10 or 15 c.c. of normal salt solution is poured into a culture tube containing a twenty-four-hour-old growth of Staphylococcus pyogenes aureus on an agar slant. The resulting emulsion is thoroughly shaken, transferred to another tube, and sedimented in a centrifuge. The upper, almost transparent, layer of the centrifugalized emulsion is pipetted off for use in the tests, since the lower opaque zone contains innumerable bacteria, many of them adhering in large, dense clumps, and therefore is unsuitable for use in the final enumeration. The proper density of the emulsion is best determined by experience, which will show that one which allows the phagocytosis of six or eight cocci by each leukocyte is easiest to work with; such an emulsion of Staphylococcus aureus should have but a delicately opaque appearance. MacFarland's nephelometer[11] may be tried as an aid in judging densities of bacterial emulsions.

III. *Obtaining the Washed Leukocytes.* At least ten drops of blood are collected and mixed in a test tube containing 2 or 3 c.c. of warm (37° C.) normal salt solution to which 1.5 per cent. of sodium citrate is added to prevent coagulation. It is important to use a solution of this percentage, which is three times stronger than originally advised by Wright and his students. A 0.5 per cent. solution of sodium citrate cannot be relied upon invariably to prevent clotting, which accident, of course, demands a repetition of this somewhat tedious step. The mixture of citrated blood is then centrifugalized until a compact corpuscular sediment, overlaid by clear citrate solution is thrown down, this sediment consisting of a deep red layer of erythrocytes, overlaid by a thin white or grayish film of leukocytes. With a suction pipette the supernanant fluid is removed down to the leukocyte film, which under no circumstance is to be disturbed. This accomplished, the layer of leukocytes and also the upper part of the erythrocyte sediment

[11] Proc. Path. Soc. Phila., 1906, ix, 65.

(say to a depth of 5 mm.) are sucked up in another pipette (Fig. 9) and blown into a small test tube, in which they are well mixed by alternate suction and expulsion with the pipette. This upper layer of erythrocytes, whose presence in the field of the stained specimen is not undesirable, also contains many leukocytes. The mixture of leukocytes and erythrocytes thus secured, known as the "leukocyte emulsion," contains a considerable quantity of the sodium citrate of the original citrated salt solution in which the blood was collected, and which it is possibly advisable to remove. To do this the citrated salt solution is pipetted off and replaced by an equal volume of normal salt solution, which is thoroughly mixed with the leukocyte emulsion so that it effectually permeates it. The mixture is then sedimented in a centrifuge, after which the first salt solution is removed with a pipette, substituted by a fresh one, and the original mixing and sedimentation repeated. The removal of this second salt solution leaves a sediment of "washed leukocytes" practically free from the anti-coagulant salt and ready for admixture with the units of bacteria and serum, in the procedure of incubation, next in order.

Having found in our late work that sodium citrate has no influence whatever on the process of phagocytosis, we now dispense with this step of washing the leukocyte emulsion, thus appreciably simplifying the technique of the test.

It is in the foregoing stage of the test that most of the mistakes and perplexities crop out, from failure to secure enough leukocytes to enable one to make an accurate enumeration of the phagocytes and their engulfed bacteria in the stained film. This failure is referable to missteps in technique relating to the primary collection of the blood, to inaccurate pipetting, and to unavoidable adhesion of the leukocytes to the inner walls of the test tube and suction tube. In collecting the blood from which the leukocyte emulsion is prepared, at least ten large drops should be allowed to fall directly from the puncture into the citrated salt solution within the test tube, the blood not being permitted to trickle down the inner wall of the tube, to which the leukocytes tend to adhere with extraordinary tenacity. To this accident we have traced several failures to find sufficient leukocytes in the stained film, notwithstanding both macroscopic and microscopic evidence of an abundance of these cells in the sediment pipetted from the layer of the leukocyte emulsion, and in spite of an otherwise adequate technique. Fewer than ten good-sized drops of blood are insufficient to yield a leukocyte film of easily workable size, for with less than this amount of blood the sediment of leukocytes is so scanty that the number of these cells which survive subsequent manipulation is too small to be taken as a basis for an accurate calculation. Inaccuracy in pipetting accounts for numerous failures, but this is a fault to be remedied only by the acquisition of a perfect technique. It need scarcely be noted, save as a warning to

the unskilled, that all the leukocytes may be inadvertently sucked up and discarded with the citrated salt solution during its removal in the step preliminary to washing the leukocytes, or that they may similarly disappear in the latter stage of the test. A test may be spoiled by neglecting to remove *all* the citrate or the salt solution above the layer of leukocytes, for in such an event the leukocyte unit will be found to consist of little else than a highly diluted collection of erythrocytes, the leukocytes being too few to be taken as the basis of a count.

IV. *Measuring, Mixing, and Incubating the Units.* A mark is made on the capillary stem of the mixing pipette about 4 cm. from its tip, the capacity of the tube between these two points being taken as the unit of volume for the patient's serum, the washed leukocytes, and the bacterial emulsion. Having placed these in their rack in the order illustrated (Fig. 1), the rubber nipple of the pipette is compressed and its point plunged into the bacterial emulsion which, by very cautiously relaxing the pressure on the nipple, is slowly sucked up to the exact level of the unit mark; the point of the pipette is then removed from the emulsion, wiped dry with a bit of cotton, and, by again carefully releasing the pressure, a small column of air is aspirated. This accomplished, a unit of washed leukocytes is similarly sucked into the pipette, then a second column of air, and finally a unit of the serum to be tested, the tube now containing equal units of bacterial emulsion, washed leukocytes, and the patient's serum, each separated by a partition of air (Fig. 10). These are now mixed by sucking them up into the expanded portion of the pipette, where they are thoroughly agitated and commingled by alternately squeezing and relaxing the pressure on the nipple, which should be manipulated with the greatest delicacy, in order to avoid sudden oscillations of the liquid and its accidental escape into the "nipple end" of the tube. When the admixture is completed the point of the pipette is sealed in a flame, after which the nipple may be removed without risk of disturbing the column of contained fluid (Fig. 11). This manner of mixing the units is preferable to mixing them according to the original technique, by alternately expelling the contents into a watch crystal and sucking them up the tube again. No better mixture is obtained by this older method, by the employment of which many leukocytes are lost[12] and myriads of small air bubbles are prone to form in the liquid, despite one's care to prevent such accidents. When sealed, the pipette is placed in an incubator, where it is kept for exactly fifteen minutes at a temperature of 37° C. A second pipette is filled in an identical manner, with equal units of the same

[12] If the contents of a pipette are blown out into a watch glass, numerous leukocytes adhere to its surface, and in consequence the mixture subsequently aspirated into the pipette and incubated is very deficient in leukocytes—perhaps so decidedly so as to preclude the possibility of making the final phagocyte count.

bacterial emulsion, washed leukocytes, and the control serum from a presumably healthy person, and incubated in the same way.

V. *Preparing and Examining the Stained Films.* After incubation the straight stem of each pipette is notched with a file and broken off, while to the other end is fitted a rubber nipple; the contents of the pipettes are then blown out upon separate glass slides or crystals

FIG. 9.—Method of aspirating the washed leukocytes.

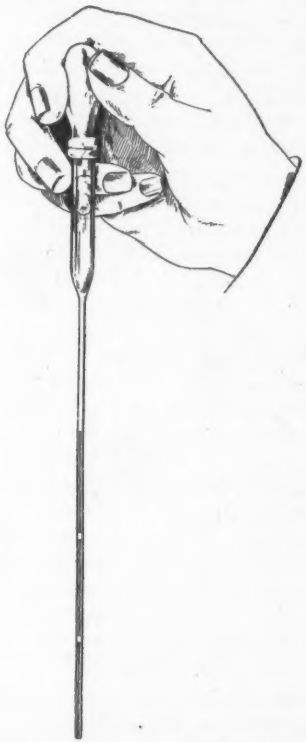

FIG. 10.—Mixing pipette containing the units of bacteria, washed leukocytes, and serum.

FIG. 11.—Mixing pipette containing the mixed units ready for incubation.

and each thoroughly mixed with a platinum loop, so as to distribute the cells throughout the fluids. Films prepared from these specimens, either with cover-glasses or with slides, according to one's preference, may be stained with any good double stain, the subsequent examination being made with a $\frac{1}{12}$ inch oil-immersion objective (Fig. 12). In our work in the Jefferson laboratory Wright's modification of Leishman's stain has given the clearest differentiation of the bacteria and their cellular assailants.

The final calculation of the opsonic index is based upon the enumeration of the bacteria found within at least 50 consecutive polynuclear neutrophiles in a film made of the specimen from the patient and in one from the control fluid. In making this estimate the bacteria simply clinging to the peripheries of the cells (not enclosed by them) were not included. Such groups of bacteria, however, were noted and recorded as "attached bacteria," for their appearance is most suggestive of an early phase of phagocytosis on the part of the leukocytes to which they adhere. The index of these extracellular bacteria is being calculated in our second series of diabetic cases, now under investigation. The two totals of phagocyted bacteria having been determined, that of the patient's specimen is divided by that of the control's, to express the opsonic

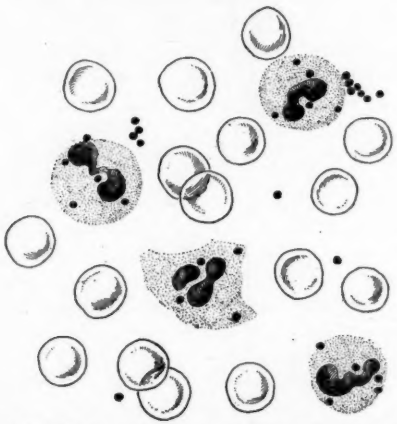

FIG. 12.—Microscopic field of a specimen prepared from the incubated units. Note the staphylococci ingested by and adherent to the phagocytes; the latter are not included in the enumeration upon which the calculation of the opsonic index is based.

index of the blood under examination. Thus if, say, 200 staphylococci were found in 50 of the patient's phagocytes and 400 in the same number of the control cells, the index for this ratio would read 0.5, or 200 to 400. It is a good plan also to calculate the percentage of phagocytic polynuclears, as advised by Simon,[13] thus obtaining an index comparable with and controlling the opsonic figure.

It will be noted that the polynuclear neutrophiles are the only variety of leukocytes taken into account in the foregoing enumeration, the number of phagocytic large mononuclear cells is so insignificant that they may be safely disregarded: only twice, during some fifty-odd examinations, have I noted phagocytosis of staphy-

[13] Jour. Exper. Med., 1906, viii, 651.

lococci by this form of the leukocyte, and in neither instance did the number of cells thus acting exceed three. It is possible, however, that with other bacteria (such for example, as the bacillus of leprosy) there may be quite a decided selective affinity on the part of these cells. Many of the eosinophiles were fragmented, clouds of granules being seen about the degenerate cell nuclei, and frequently lying in close contact with the bacteria free in the plasma. At first glance this reminds one of Kanthack and Hardy's description of the eosinophiles in lymph inoculated with anthrax bacilli, in which experiment it was found that the bacteria were primarily attracted by the eosinophiles, which, coming in contact with the germs, discharge their granules about them, with apparently crippling effect, since the bacilli soon show degenerative changes and later become the prey of the phagocytic large hyaline cells. It is, of course, far-fetched to attempt to distinguish any such phenomenon in the opsonin specimen, though the presence of free eosinophile granules near unengulfed bacteria in these films suggests more than a merely traumatic fracture of this peculiarly fragile type of cells, with the accidental grouping of their escaped granules in the neighborhood of the staphylococci.

In summing up the clinical value of the opsonin test, one may regard it as useful in two distinct ways: as a diagnostic agent, and as a means of gauging the effect of the vaccination method of treating certain infectious diseases. As a diagnostic agent the test should not, of course, be exploited in diabetes; nor, indeed is an additional aid of this sort necessary in this condition. A diabetic's opsonic index, however, gives a clear idea of the patient's resisting powers, of his susceptibility to secondary infection, and of the gravity of the inroads made by the disease. On the contrary, the opsonin test appears to be of considerable utility in the recognition of early tuberculosis, for in this infection the index to the tubercle bacillus is found to be either very low or excessively high; the former suggests at least a predisposition to the disease, while the latter points to an actual infection against which the subject's resisting powers are raised in defense. In an obscure case, an index to the tubercle bacillus ranging between 0.6 and 1.3 is a significant corroboration of otherwise puzzling symptoms. In still another manner is the opsonic index helpful in detecting such cases. The index of a normal person who has been injected with a small dose of tuberculin R. falls moderately for a period of about two days, after which it rises somewhat above normal, and finally returns to the original figure. In a tuberculous subject a similar injection is followed by a much more decided drop in the index, which remains subnormal for a week or so, and does not regain its original height for a fortnight or more. The fact that tuberculous effusions show a lower opsonic content than the subject's blood serum may also prove of diagnostic utility, as, for example, in determining the character of pleural or peritoneal exudates.

The most practical value of the opsonin test lies in its application to the vaccination method of treating bacterial infections, for in this class of diseases both the proper dosage of the vaccine and its effect upon the patient's powers of reaction are determined by the behavior of the subject's opsonic index during the period of treatment. Of this we are convinced, from personal knowledge, notwithstanding the criticisms which have recently been aimed at the test. This method of treatment, so ably devised by Wright and his pupils, is based upon the fact that the opsonic powers of the blood can be increased by the injection into the human body of vaccines, the essential steps being as follows: (1) Isolation of a pure culture of the bacterium responsible for the infection; (2) estimation of the patient's opsonic index toward the microörganism thus recovered; and (3) inoculation of the patient with suitable doses of vaccine prepared from this microörganism, in case the index be found subnormal. By this method of treatment it is possible, in many infections, to raise low opsonic indices to constant, high levels, and, in consequence of the habitual, active phagocytosis thus excited, to ensure disposal of the invading bacteria, and, hence, the recovery of the patient. That this may be done is shown by the numerous reports made during the past year, especially by those of the British school, whose treatment of acne, furunculosis, and abscess by staphylococcic vaccine, of malignant endocarditis by streptococcic vaccine, and of tuberculous diseases by tuberculin gives promise of even more favorable results in the future.

CHRONIC INTESTINAL AUTO-INTOXICATION.

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Intestinal auto-intoxication may be defined as that condition in which toxins formed in the intestines are absorbed by the organism in which they are produced. The use of this term has been objected to and enterotoxismus, or intestinal toxemia, has been suggested in its stead. Strictly speaking only that process should be called auto-intoxication which is caused by the toxic bodies resulting from metabolism and not due to any exogenous cause, such as bacterial activity. For the infectious process the term auto-intoxication is certainly inappropriate, but for the others Albu claims that they can be looked upon as autochthonic, in that they are caused by saprophytes which act only within the organism under special conditions. For the present, at least, it is impossible to determine which toxic bodies are the result of metabolism alone or the combined result of

various causes. Moreover, the term intestinal intoxication is used by the French, the Italians, the Germans, and by ourselves, and it would seem that when the time comes that we can draw distinct lines between the various forms of intestinal intoxication it will be time to add new terms to our complicated terminology.

The whole subject was first brought to the general attention of the profession by Bouchard in 1887, and while much has been discarded which he claimed, yet much of the impetus given to the study of this subject is clearly due to the publication of his fascinating little book.[1] Unfortunately the most important and characteristic of his symptoms, the toxicity of the urine, was not verified by subsequent observers (Albu, Forchheimer, and Stewart); so that, while such a clinical entity as chronic intestinal auto-intoxication was accepted, other proofs had to be found for its existence.

From a chemical point of view chronic intestinal auto-intoxication is due principally, if not entirely, to the intestinal changes in albumin and in nuclein. The changes in these two substances are the result of the activity of enzymes or of bacteria. The substances produced by enzymes are albumoses from albumin and the xanthin bases and uric acid from nuclein. In both instances pancreatic digestion is the principal cause. The action of bacteria manifests itself only upon albumin, as far as we know, in the form of pancreatic putridity and the bacterial processes which go on in the colon. The substances which result from this process and which interest us are phenol and indol, Brieger having shown that the rest of the bodies formed during putridity of albumin are little toxic. It has been shown that some of the albumoses formed during digestion are toxic, that is, when injected into lower animals. Of the purin bodies xanthin, hypoxanthin, paraxanthin, hetroxanthin, and adenin have also been shown to be toxic. Uric acid is toxic in a certain sense only; when it is injected into animals in large quantities no toxic symptoms are produced, but local symptoms may result under favorable circumstances. Both phenol and indol are toxic; in the lower animals indol produces decided symptoms (Herter); as the production of phenol and indol usually go hand in hand, the determination of one is sufficient for clinical purposes in order to determine the amount of putridity in the intestine.

As all processes due to enzymes are of relatively short duration, we are justified in assuming that all changes due to enzymes are completed in the small intestine, and this may also be the case in connection with uric acid and the xanthin bodies. As far as putridity goes, under normal circumstances little or none is found in the small intestine; indeed, Kohlbrügge says that the empty small intestine may not contain any bacteria. In the lower part of the ileum and in the colon, however, we find a large number of bacteria,

[1] Lecons sur les auto-intoxications dans les maladies.

and here is found the place where putrefactive changes take place. Not only the mere presence of bacteria, but the comparative lack of motion, therefore the greater the length of time in which these bacteria can act upon albuminous substances, makes it reasonably certain that putrefactive changes are confined to the colon under normal conditions. In the human being it does not take longer than a few hours (Krehl) for the small intestine to empty itself into the colon, so that we find everything which has not been absorbed by this time in the colon, including the metabolic products of nuclein, the xanthin bases. If for one reason or another the colon is not emptied sufficiently, a greater chance both for formation and for absorption of toxic bodies is given than when such a condition does not exist. From the intestines these various substances are absorbed and are sooner or later found in the blood, unless they are converted into harmless combinations. Those substances that are absorbed by the blood enter the liver and are subjected to oxidation, the so-called "filtering function" of the liver. Those that find their way through the lacteals are bound or changed by the lymphatic nodes through which they must pass.

As a result, a number of these toxic bodies are then rendered inert; some lose a part of their toxicity, others may pass through unchanged. In following the course of the circulation some of these bodies are excreted by the lungs, but relatively few, and then enter the left heart, going eventually to the kidneys, where many leave the body. Herter has shown that the cells of the liver, the kidneys, the muscle, the blood, and the brain have a decided effect, in the order mentioned as to quantity, upon a change in phenol and indol; so that the toxicity is being reduced all the time. During the circulation arterial blood containing toxins may be distributed to many parts and organs, the mucous membranes, the central nervous system especially, and may be eliminated there, producing symptoms or lesions. After the blood has come back to the right heart it has then been changed, as to these toxic bodies, depending upon the activity of the liver, the kidneys, the lungs, the muscle, the blood—probably by all the cells in the body. Two eventualities arise: either the toxic substances have all been removed, or this has not been accomplished. The latter is due either to a relative or an absolute insufficiency of the toxin-destroying organs or cells; relative in that the amount of toxin is too great; absolute in that for some reason the organs or cells do not perform their normal function. But after a time it does not remain a question of function alone; organic changes take place, either on account of increased functional activity, as upon elastic tissue, or because of irritation, as by the purin bodies, Gaucher, Crofton, Kolisch, Minkowski showing that they produced actual lesions in the kidneys.

For practical purposes the amount of toxic bodies formed depends upon the nature of the food, upon the time it remains in the colon,

and the character of the processes within the intestine. Except in abnormal conditions the processes are the same, provided the other two factors are unchanged, for within certain limits the bacteria are the same. Under abnormal conditions the flora may be changed and then we may have peculiar auto-intoxicative bodies formed of which we know very little. Under all circumstances it is important to consider the time which is afforded the bacteria to act upon the contents of the colon, and the slow peristaltic function of the large intestine increases the activity of these bacteria in that they are not disturbed by motion. The character of the food limits the quantity and the quality of changes, but more or less putridity will always be found as the result of normal metabolism.

Turning to the practical aspect I desire to call attention to an analysis of 77 cases examined by ordinary clinical methods in which, as I believe, intestinal auto-intoxication was present. All the patients were observed in private practice. Children are excluded because the clinical picture in them differs very much from that in the adult. Of the 77 there were 37 males and 40 females, 43 patients being between thirty and fifty years of age, 48 having good habits, 12 being overworked, 10 irregular habits, 3 alcoholics, and 4 ex-cessive smokers. Their occupation was very varied Of the women, 31 were housewives; of the men, 16 were merchants; the professions were represented by 2 physicians and 2 lawyers. There were 3 farmers, 7 salesmen, and 1 broker. As all belonged to the so-called better classes whatever effect occupation may have had is not shown in this collection of cases. I have analyzed the chief complaints of these patients and find that they were general in 12 cases; 18 had some form of stomach trouble, 12 had intestinal and 52 had nervous troubles, 4 genito-urinary symptoms, 4 skin troubles, 17 some trouble with the locomotor apparatus, and 7 troubles with nose, eyes, or ears. Among the general troubles 8 complained of loss in weight, 3 of general debility, only 2 complained of their mouths and they had been sent by dentists for general treatment. Among those having gastro-intestinal troubles 2 complained of bilious attacks, 6 of constipation, 3 of alternate constipation and diarrhœa, and 2 of flatulence. The fact that only 11 patients should have complained of intestinal symptoms is one that will be referred to later. The great number of principal complaints were referred to the nervous symptoms, and here we find 7 cases of migraine, 17 with headaches, 6 with neuralgias, and 6 with vertigo.

The general appearance was good in 54 patients, not good in 21, and 10 were obese. In 14 of those noted as not good, the expression anemic was used, the other 7 were badly nourished, 1 having a cachectic appearance due to prolonged suffering from migraine plus morphine.

In the special examination I note only the salient points, as it would lead us too far to go into more minute detail. In the mouth we find Riggs' disease in 66 cases, normal mouth in 8, and no teeth

in 3, therefore no Riggs' disease. Riggs' disease is called by various names: pyorrhea alveolaris, gingivitis interstitialis or parenchymatosa, stomatitis ulcerosa chronica. In a former publication upon the subject I suggested the latter name and divided the disease into three stages: (1) In which there is only the necrotic seam at the margin of the gum; (2) in which there is denudation of the teeth; and (3) in which there is pus infection. There were 21 in the first stage, 40 in the second, and 5 in the third. The fact that there were only 5 in the third stage is readily explained in that, as a rule, patients in private practice take good care of their teeth and certainly keep their mouths as aseptic as possible. As for the frequency of this manifestation in the mouth in chronic intestinal auto-intoxication, if we are at all upon the right track as to our understanding of the process in the intestine the existence of such large numbers of cases of Riggs' disease is almost a logical consequence. We have seen how the purin bodies are found in the intestine; we know that they produce necrosis of tissue; we have necrosis of tissue in Riggs' disease and in a large percentage of cases we find uric acid in scrapings from the teeth—so often has this been found to be the case that this form of disease has been called gout of the teeth. That this is the case I am prepared to testify as the result of a large number of examinations of scrapings from the teeth, the so-called blood calculi, in which I have always found uric acid. On the other hand, I should not like to be understood as saying that only the purin bodies, especially uric acid, may produce Riggs' disease.

Of the 77 patients 54 had stomach symptoms, 23 had none; 27 had dyspepsia, 19 had hyperchlorhydria, 1 achlorhydria, and 4 had other gastric neuroses, sensory or motor. In 7 patients there was nausea or vomiting and 1 had gastroptosis. Any explanation for the frequency of stomach symptoms in connection with chronic intestinal auto-intoxication must be purely hypothetical, as very little has been done to demonstrate which bodies are eliminated by the stomach; certainly nothing has been done, as far as I know, in connection with the various substances which interest us. This we know, that certain substances when introduced into the circulation are eliminated by the gastro-intestinal tract: thus the cholera toxin is formed in the intestine and is partly eliminated in the stomach from which it is removed by vomiting as Alt has shown. It is possible that the various substances formed in the colon may be eliminated into the stomach and there produce either functional or organic disturbance. But it is also possible that the nervous disturbance which exists to a great degree, as has been shown in intestinal auto-intoxication, may be the cause. Finally, the fact must not be lost sight of, that gastric disturbances, provided there be diminished HCl secretion plus deficient motility, may increase intestinal putridity. (Krehl.)

When I came to question and examine the 77 patients I found that

all except 4 presented evidences of some trouble in the bowels. Eighteen were regular in their evacuations, 4 irregular, 44 constipated, that is, not having a movement daily, 5 had diarrhœa, in 5 there was alternate constipation and diarrhœa; 3 suffered much from flatulence and colic, and 5 had enteritis mucosa. That so many were found constipated is not an uncommon experience, for unless questioned about it many patients are apt to be silent on the subject. In examining the patients the history of 10 cases of appendicitis was elicited, 4 having had severe attacks from five to twenty years ago, 2 having the relapsing form, and 4 chronic appendicitis; 5 of these cases have since been operated upon and some of the conditions to be described were verified in them. The constipation which was present in them undoubtedly produced the symptoms of auto-intoxication, as these have disappeared since the operation of appendectomy. The alterations due to appendicitis seem to produce changes in the cecum which are followed by lack of peristalsis. One patient had a dilated colon, in 3 there was Glénard's disease.

In examining the colon by percussion and by palpation it was found that one or another part of it was filled in all but 4 cases; most commonly it was at the sigmoid flexure and in the descending colon, next in frequency came the transverse colon, then the cecum and ascending colon, and finally the hepatic and splenic flexures, that is, without any other part being involved. As a rule, we find combinations of several parts sometimes, as in 13 of the cases the whole colon was filled up. The most reliable results are obtained, by percussion, when the patient is in the upright position; for palpation the patient should be upon the bed; not infrequently it is necessary to turn him from one side to another or to lower the trunk. In making this statement I am fully aware of the untrustworthy results obtained from the percussion of the intestines in general, but here we have a something within the intestines which produces dulness when lightly percussed and whose presence can be verified by palpation. It is not safe, however, to trust percussion or palpation for a final opinion until further observation of the patient has taken place.

In order to be sure of the condition the fecal material must be removed from the colon in one way or another. In many patients this is not easily accomplished, as the fecal material has remained in the colon for a long time. In those patients having diarrhœa the diarrhœic material has passed without disturbing the old fecal material. It may be well to state that old fecal material does not produce auto-intoxication, but the condition of the bowel which results from it does. That the observations recorded above, as to retention in the colon are correct can be verified by successive and continuous examinations. Many of the patients when relieved either give up the treatment or neglect themselves in other ways; when they come back for observation the retained material is found

in the same place where it was first detected. After the bowel has been thoroughly cleaned out it is then either found empty, *i. e.*, no dulness on percussion and no resistance on palpation, or there is resistance showing that the bowel wall is changed. According to my experience an empty bowel cannot be felt, as first claimed by Glénard and repeated by Sahli. When the bowel can be felt in the majority of cases its wall is thickened; this thickening may be due to a spastic condition, as suggested by Osler, or to a lesion due to a chronic catarrhal condition and infiltration of the walls of the intestine. When, after the removal of the collected fecal masses has been accomplished, no thickening of the intestines is found after repeated examination, we are justified in assuming that the fecal masses accumulate in the same place because peristalsis does not take place there; therefore an atony of the intestines. If, on the other hand, the thickening is found, and this usually occurs at the sigmoid flexure, there is some change in the bowel wall. In the greatest number of cases no thickening is left; therefore, a process due to faulty innervation, or atrophy. When the thickening is left, therefore, I believe it to be due to an organic process, a fact which is more definitely proved by the results of treatment than in any other way.

Before leaving the abdominal organs I wish to add that 3 of the patients had enteroptosis and 1 a fibroid tumor of the uterus, in which cases the interference with peristalsis was purely mechanical. In only 3 patients was the liver found enlarged.

The routine examination of the urine showed some changes which are worthy of special attention. The specific gravity showed nothing of importance, one-half of the cases being between 1009 to 1022, the other half above 1022 to 1030. Albumin (heat and nitric acid contact tests) was found in 6 cases. Indican was found increased in 68 cases. Obermayer's test was used: strong HCl, sp. gr. 1.19, to which is added 4 grams of ferric chloride to the liter. This we have used as a comparative test, by the adoption of a color scale. Simon has shown that indicanuria goes hand in hand with phenoluria, so that indican can reasonably be looked upon as an index to the amount of putrefaction which goes on in the colon. All the recorded cases were on mixed diet and had no other conditions which would produce an increase in indican elimination. It will be interesting to compare the increase in indican with the symptoms and the results of the physical examination. Of the 44 cases which were constipated 39 presented increase in indican. As far as this observation goes, it is in direct refutation of the statement made first by Jaffé in 1877, and since repeated by every author whom I have been able to consult. The case which Jaffé reports is not one which can carry much weight with it in evidence of his assertion in that it was one of intestinal obstruction of the colon. Curiously enough in the same volume of Virchow's *Archiv* there appears another article on

the detection of the conjugate sulphates in the urine by von Velden,[2] in which the analysis shows that in one case of constipation the indican was increased. Baumstark has reached the same conclusion.

In all the cases in which there was alternate diarrhœa and constipation the indican was increased whether examined during the period of diarrhœa or of constipation. All the cases of mucous colitis had increase of indican. In the 13 cases in which the whole colon was found filled we found, on an average, the largest quantities of indican. Next to this came the sigmoid flexure and then the descending colon.

Microscopically there was found in the urine oxalate of calcium in 33 cases, uric acid in 11 cases, amorphous urates in 5 cases. Red corpuscles were found in 18 cases; it is difficult to account for their presence, sometimes only a few corpuscles, sometimes many were found. The subject is now being investigated, but for our purpose it is of interest to note that in 11 of the 18 cases oxalate of lime was also found. Hyaline cylindroids were present in 8 cases, hyaline casts in 15 cases, fine granular casts in 10 cases, once combined with hyaline casts, and once epithelial casts were present. The hyaline casts were found with albumin in the urine in 3 cases. It is interesting here to consider Dreser's statement that in all cases in which indican is increased there is albuminuria, because it produces irritation of the uriniferous tubules after having been taken up by their epithelial cells. We have 68 cases of increase in indican and only 6 cases of albuminuria. As far as the presence of hyaline casts is concerned, out of 15 cases we find 10 in which there were present large quantities of indican, the other 5 representing moderate increase. Only 1 of the cases in which albuminuria and casts were found is a chronic nephritic.

One other condition requires especial notice in that it occurred in 28 cases. These patients very frequently volunteer the statement that they have to pass large quantities of urine at times and frequently and in the course of the same day this condition may change to an oliguria. Or the condition of polyuria persists and is then followed by an oliguria, the one alternating with the other. This condition of polyuria may be ascribed to nervous processes, which, as will be shown, are very commonly associated with auto-intoxication. But the polyuric urine is most commonly of low specific gravity and in it the greatest quantities of indican is found. The oliguric urine, on the other hand, is of higher specific gravity and contains less indican; it would seem, therefore, that the indican acts, when present in large quantities, as an irritant to the kidneys.

In the women 18 of the 40 were afflicted with some abnormal form of menstruation; 13 had dysmenorrhœa, 3 menorrhagia, 2 insufficient and irregular menstruation. In a large number of these

[2] 1877, p. 343.

cases the same cause which produced the menstrual changes may be considered as the cause of the intestinal auto-intoxication; displacements, ovarian inflammations, peri-uterine inflammations, etc., in that the normal function was mechanically interfered with. But there remains a number of cases in which the gynecologist finds nothing wrong. In these cases it would seem that some toxic body may be also eliminated by the mucous membrane of the uterus; that substances are eliminated here can be easily demonstrated by testing the cervical mucus for iodine when the patient takes iodide of potassium.

Nervous symptoms were present in 61 patients. Of these there were 6 genuine migraines. All of these had large quantities of indican, 4 had constipation, 1 loose passages, and the others alternate loose and constipated movements; 2 had appendical troubles, 1 had a dilated and filled cecum, 2 sigmoid flexure trouble, and 1 descending colon and sigmoid flexure thickening; 31 patients had headaches, all of them had indicanuria except 3. All of them except 4 had some change in the bowels. Neuralgias were present in 11 patients—2 were noted as neuritis; 4 had paresthesia; 14 were nervous and restless; 7 irritable and excitable, with or without other symptoms of neurasthenia; 7 had depressive symptoms, 3 phobias, 11 insomnia, 2 hypochondriasis, and 1 melancholia; 4 were hysterical. Vertigo was present in 11 patients.

In 58 patients some deviation from the normal was found in the cardiovascular apparatus. Neuroses were found in 17; 11 had myocardial conditions; 6 chronic myocarditis, 3 dilated hearts, 1 the heart of arteriosclerosis, and 1 obesity of the heart; 12 had valvular lesions, 4 aortic insufficiency, 5 mitral insufficiency, 1 mitral insufficiency and stenosis, and 1 aortic and mitral insufficiency. In 3 others there was heard a soft systolic aortic bruit and in 5 there was an accentuation of the second aortic sound. There is no doubt in my mind as to the connection between neuroses of the heart and chronic intestinal auto-intoxication. That chronic myocarditis is produced by toxemia is still a matter of discussion. For the valvular lesions we could only be justified in considering those due to an intestinal intoxication which are combined with arteriosclerosis, that is, those mentioned last. Eighteen patients had arteriosclerosis. The discussion of the relation of intestinal auto-intoxication to arteriosclerosis would lead us too far from our subject. That arteriosclerosis is produced by gout is admitted, that gout, in so far as purin bodies are concerned in its production, is the result of intestinal auto-intoxication may also be admitted. How this produces arteriosclerosis has not been demonstrated, as it has been done with adrenalin and nicotine.

In analyzing the symptoms on the part of locomotor apparatus we again come to the question of gout, but here in a more definite form. In 50 patients there were found symptoms or diseased con-

ditions in the joints or muscles. Of these 19 had gouty joints, 24 had muscular rheumatism, 13 complained of rheumatic, muscular pains which were transitory. One patient had intermittent hydrarthrosis of the knee. Out of the 19 with gross manifestations of gout 15 had increased indican. The formation of uric acid, and its antecedents, in the intestine evidently depends upon some of the same conditions that favor the formation of indican, that is, the quality of the food and the time required until it leaves the colon. Of the 24 who had muscular rheumatism 20 had indicanuria, the average being 3.5 with a maximum of 5 in 1 case. Transitory pains, muscular or otherwise, represented 11 cases of indicanuria out of 13; 22 cases presented skin manifestations; 5 urticaria, 5 eczema, 3 furunculosis, 4 acne vulgaris, 1 angioneurotic œdema (feet, toes, face; red spots), 1 dermatomyositis, and 1 with erythemata. One of the patients had red axillary perspiration and in 1 there was herpes zoster. Of these urticaria, eczema, erythema, and acne vulgaris have been ascribed to intestinal auto-intoxication as a direct or predisposing cause.

Only 13 patients had respiratory troubles; of these 5 had tuberculosis, 2 bronchitis, 4 bronchitis and asthma, and in 2 there was also emphysema.

The blood, when it was examined, presented the ordinary picture of a chlorotic anemia, with the exception of 3 cases, which will require further study.

The number of cases in which the nose, the eyes, and the ears were affected, that is, the mucous membranes, is small, principally because no note was made of their presence or absence unless there were special reasons for doing so. There were 6 cases of tinnitus aurium and 3 cases of Ménière's disease in which chronic auto-intestinal intoxication was found. In addition there was a number of nose, pharynx, and eye conditions which require further study, but which also seemed to be connected with auto-intoxicative processes.

If we now try to get a composite clinical picture from what has been said, in order that the diagnosis of chronic intestinal auto-intoxication may be made, the following will have to be taken into consideration:

1. In the gastro-intestinal tract there are Riggs' disease, various forms of stomach troubles, change in functional activity of the colon, and demonstrable retention of feces due to one cause or another.

2. In a large percentage of the cases indican is increased in the urine, and a microscopic examination shows, again in a large percentage of cases, calcium oxalate (50 per cent.), uric acid and urates (25 per cent.), red corpuscles (about 30 per cent.). In 28 cases, about $33\frac{1}{3}$ per cent., the alternation of polyuria with oliguria was noted.

3. One-half of the females had menstrual trouble.

4. Next to Riggs' disease, nervous symptoms were present in the

largest number of patients. Of these 31 of the 77 patients had headaches.

5. In a large number (58 out of 77) cardiovascular changes were observed; over one-half were due to neuroses and to myocardial conditions.

6. Of the 77, 50 patients had locomotor symptoms, gouty joints, but especially muscular symptoms.

7. Twenty-two patients had skin lesions.

From the combination made by various symptoms, the diagnosis of chronic intestinal auto-intoxication should be easily made, and, as a matter of fact, this is the case in practice, as is shown when this diagnosis is followed by the logical therapeutic pressures.

But it is much more difficult to determine how much importance the intoxication may be in an individual case—whether it produces all the symptoms, whether it is the cause or the result of other conditions, whether it is the direct or the predisposing cause. It is a great temptation to make this diagnosis, as it is to make all diagnoses that can be so generally applied as this one. Therefore the utmost self-criticism should be used before chronic intestinal auto-intoxication should be looked upon as the final diagnosis. In these cases which I have collected this diagnosis was made only ten times. In all the other cases the auto-intoxication was looked upon simply as a contributory cause, present and requiring treatment possibly, but not the principal disease.

THE AUSCULTATORY AND PERCUSSION FINDINGS OF THE HEART IN LATE CHILDHOOD.

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There is probably no period of life in which the heart findings during physical examination are more frequently misinterpreted and consequently misjudged than in late childhood. This seems to depend on two factors: (1) The comparatively large cardiac area; and (2) the frequency with which murmurs are heard over the heart at this time. With these points in view, a number of children, not patients, were examined. The results obtained in 100 of these, free from cardiovascular or renal disease, anemia, or abnormal abdominal conditions or distention, are given herewith.

Before presenting an analysis of the examinations an explanation of the plan adopted in calculating the cardiac outline seems necessary. Palpation and percussion were employed, and the lines of deep cardiac dulness were taken. These are more easily outlined in children than in adults, for reasons well known; namely, the thin chest wall, the thin layer of lung tissue overlying the heart,

and the less independent vibration of the sternum and anterior thoracic wall during percussion. These factors also account, to some degree, for the larger cardiac area in children.

The upper and right borders were obtained in the erect, and thereafter in the recumbent position. The left border was similarly obtained when the apex beat was not distinctly evident or palpable. While the apex beat does not always represent the extreme left limit, it, in general, will give, I think, more accurate results than percussion.

The ribs and interspaces were regarded in estimating the upper border and the sternal and nipple lines, respectively, in calculating the right and left borders. While the nipple may vary in position, I think the mammillary line will prove quite as accurate as the lines that may be dropped from the clavicle, in determining the midpoint of which undoubtedly greater errors are possible. On the other hand, measurements of distances of cardiac area to the left from the median line were not employed, because this does not convey a practical conception of the subject. The children studied had passed the sixth year and were of varying ages up to puberty.

By percussion in the parasternal line the upper border was found in the erect position, as follows:

Location.	*Number of children.*
On the second rib	1
In the second interspace	4
On the third rib	65
In the third interspace	17
On the fourth rib	13

The right border, obtained on a level with the fourth rib and the fifth interspace, in the erect position, was found:

Location.	*Number of children.*
On the left sternal border in	3
In the mid-sternal line in	12
On the right border of sternum in	8
0.5 cm. to the right of the sternum in	13
1.0 cm. to the right of the sternum in	32
1.5 cm. to the right of the sternum in	18
2.0 cm. to the right of the sternum in	14

The dulness obtained to the right of the sternum is always slight, and is brought out only by light percussion. Heavy percussion may bring out dulness beyond the actual heart outline in a child (Sahli).

The apex beat in the erect position was located with regard to the nipple line, as follows:

	Number of children.		
Location.	*Inside N.L.*	*On N.L.*	*Outside N.L.*
In the fourth interspace	3		3
In the fourth interspace and behind the fifth rib	3		
In the fourth and fifth interspaces			1
Behind the fifth rib	4	4	2
Behind the fifth rib and in the fifth interspace	4		
In the fifth interspace	52	19	5
In the fifth interspace and behind the sixth rib	1		
Behind the sixth rib and in the sixth interspace			1

The upper border in the dorsal position was:

Location.	*Number of children.*
Unchanged in	45
Elevated the width of an interspace	19
Elevated the width of a rib	11
Elevated the width of a rib and an interspace	5
Dulness noted as more pronounced in	3
Dropped one interspace in	3
No record in	14

The right border in recumbency was:

Location.	*Number of children.*
Unchanged	43
Diminished 0.5 cm.	13
Diminished 1 cm.	16
Diminished 1.5 cm.	5
Dulness noted less marked	10
No record	13

The apex in recumbency was:

Location.	*Number of children.*
Unchanged	57
Elevated from the fifth interspace to behind the fifth rib	13
Elevated behind the fifth rib and into the fourth interspace	4
Elevated from the fifth to the fourth interspace	4
Less distinct with position unchanged	8
Shifted to outside nipple line with horizontal position unchanged	7
No record	14

Symington, in discussing this question from an anatomical point of view, states that since the vertical extent of the heart in relation to the anterior chest wall is practically similar in children and adults, it naturally follows that the transverse diameter of the heart, as compared with that of the chest, is relatively greater in the former (in whom the characteristic feature of the thorax is its narrowness) than in the latter.

The average diameters of the thoraces of the children examined, taken in the upright position, were as follows:

Age	*Lateral diameter.*	*Anteroposterior diameter.*
7 years	6.500 inches.	5.625 inches.
8 "	7.125 "	5.650 "
9 "	7.530 "	6.053 "
11 "	8.060 "	6.150 "
12 "	8.600 "	6.620 "
13 "	8.480 "	6.500 "
14 "	8.700 "	66.500 "

Contrary to the observations of Gordon, who found a decrease in the anteroposterior diameter in the dorsal position, I found either a slight increase or no change in this diameter in recumbency, only occasionally noting a slight decrease. Mathes records similar results in his article on enteroptosis.

Gierke took measurements of the length of the heart from the apex to the middle of the right border (which latter was represented

by a line drawn from the upper point of the heart in the middle line on a level with the second rib to its lower border to the right of the middle line), in addition to measurements of the lateral diameter of the chest. I quote only those examined over six years.

Age.	*Lateral diameter.*	*Heart's length.*	*Per cent. of heart's length of lateral diameter.*
7 years	14.00 cm.	9.0 cm.	64
8½ "	18.00 cm.	9.5 cm.	53
9 "	19.00 cm.	10.0 cm.	52
9¼ "	16.50 cm.	12.0 cm.	72
9½ "	18.25 cm.	9.5 cm.	52
9¾ "	19.00 cm.	10.0 cm.	52
10 "	15.00 cm.	11.0 cm.	73
10 "	20.00 cm.	12.0 cm.	60
10¼ "	17.00 cm.	9.0 cm.	53
10½ "	16.00 cm.	10.0 cm.	62
11½ "	18.50 cm.	12.0 cm.	66
12 "	16.75 cm.	10.0 cm.	59
12¾ "	20.00 cm.	10.0 cm.	50
13 "	19.00 cm.	10.5 cm.	55

Of the children examined by Gierke, it will be noted that the length of the heart was equal to the percentages given of the lateral diameter varying from 50 to 73 per cent. The measurements of heart length, however, are not parallel to the transverse diameter, the former being at an angle of about 25° to 30°. The above represent individual cases and not averages of a number of cases.

While a verification of my findings by the *x*-rays would be desirable, this, for evident reasons, was found impractical. I might mention, however, as a basis of comparison, the findings of Dusch and Steffen. Dusch states that the apex may be found inside, outside, or in the nipple line; that the left border extends slightly beyond the apex; that the right border projects a little to the right of the right sternal border; and that the upper border is found in the second interspace or behind the third rib. Steffen found the right border 1 to 3.75 cm. to the right of the middle line on a level with the fourth interspace and fifth rib.

It will be noted that if we combine the more definite parts of Dusch's statements with those of Steffen, they represent closely my findings.

To sum up the findings of the 100 children examined, it may be stated that the upper border percussed in the parasternal line is most frequently found on the third rib, less often in the second or third interspace; that the right border may extend 0.5 to 2 cm. to the right of the sternum, as indicated by a slight relative dulness only; and that the apex, while most frequently found in the fifth interspace inside the nipple line, may be found outside of it. It is seldom in the fourth interspace, in which event it is as often inside as outside of the nipple line.

It will be noted that in changing from the erect to the dorsal position no change is found in the level of the upper or right border

in about 45 per cent. of the children, and that in many of the remainder a difference of 0.5 to 2 cm. was found either in elevation of the upper border, or diminishing of the right border, there being no parallelism in the changes in these borders in most of the children.

In a few children the upper border was lowered in the recumbent position. In regard to the position of the apex, in more than half it remained unchanged, though at times it became less distinct; in others it ascended the width of an interspace or a rib, or of both; and in a few instances, without change in horizontal level, it glided slightly to the left.

The differences in the cardiac area, as found in the erect and the recumbent positions, undoubtedly depend upon the two factors often cited: elevation of the diaphragm and gravity.

The importance of an accurate knowledge of the area of cardiac dulness in children might not be apparent were we to neglect to study at the same time the auscultatory findings. I have, therefore, attempted to tabulate some of the results:

Auscultation was carried out in the erect and in the recumbent position. Of 94 cases in whom the tones were noted the—

	Number of children.
First tone at the apex was louder standing in	59
First tone at the apex equally loud or louder in recumbency in	35
Second tone at the apex was louder than the first tone in erect position in	5
Standing.	
Pulmonic tone was louder than aortic in	65
Aortic tone was louder than pulmonic in	21
Pulmonic and aortic tones were equally loud in	8
Recumbent position.	
Pulmonic tone was louder than aortic in	77
Aortic tone was louder than pulmonic in	4
Pulmonic and aortic tones were equally loud in	13
The first tone appeared at times divided in	12
The second tone at the apex appeared divided in	1
The second pulmonic was divided in	12

ACCENTUATION OF SOUNDS.

Standing.		*Reclining.*	
Pulmonic.	*Aortic.*	*Pulmonic.*	*Aortic.*
4	2	5	0

Murmurs in the cardiac area were heard in 64 cases. Of this number in only 18 were they heard in the erect position, leaving 46 in whom they were audible only in recumbency. Murmurs heard in the erect persisted in the recumbent position.

In the 18 children referred to the murmurs were always systolic in time and localized as follows:

Location.	*Number of children.*
At the apex in	2
At the apex and the base in	6
At the apex and the pulmonic area in	2
In the pulmonic area only in	6
In the pulmonic and aortic areas in	2

The localization of the murmurs which were all systolic in the 64 children in whom they were heard in recumbency was as follows:

Location.	*Number of children.*
Over the apex only in	3
Over the apex and pulmonic areas in	17
Over the apex and pulmonic and aortic areas in	25
Over the pulmonic and aortic areas in	8
Over the pulmonic area in	7
Over the apex and aortic areas in	2
Over the aortic area in	2

The murmurs were much influenced by position: those heard over the apex and the pulmonic area were usually intensified on placing the child on the left side, and were well heard along the left limit of the heart; when the murmur was heard only over the apex or the pulmonic area it often appeared at either point when not previously heard. Occasionally the murmur was little affected and was even diminished in the left position.

On the other hand, in the right lateral position, the murmur sometimes appeared along the right side of the sternum and was louder over the aortic area than in the dorsal position; in a few children it occurred for the first time over the aortic area under these conditions.

In one child, after distention of the stomach by gas, a systolic murmur appeared over the base of the heart. In a few instances the murmur seemed intensified after inflating the stomach.

Steffen mentions a case in which a systolic murmur was heard over the heart on pressing an enlarged liver upward. He attributed it to direct compression of the heart.

The murmurs varied considerably, at times, in loudness under the auscultating ear, were sometimes inconstant, and frequently disappeared at the height of inspiration or were greatly diminished in intensity, being usually heard best during the expiratory phase; they were also heard well during the ordinary respiratory excursions. They were seldom heard much beyond the cardiac area, were usually loudest over the pulmonic area, but not infrequently so over the apex. They are not loud murmurs, as a rule, and are sometimes so low as to be easily overlooked.

From the mentioned characteristics of these murmurs it is evident that they do not conduct themselves as do organic murmurs, which are not markedly influenced by position or the respiratory movements. We must, I think, look upon them as accidental murmurs, and accidental murmurs of striking similarity, often induced and almost always influenced by position and respiration, all of which suggest that they are dependent on the relation of the heart to its environment, that is, the lungs, or *vice versa;* in other words, we are dealing with extracardiac, paracardiac, or cardiopulmonary murmurs, occurring in the systolic phase of the heart cycle.

It may be assuming considerable to state that all these murmurs were cardiopulmonary, but in all those instances in which position

and respiratory movements exerted such a marked effect (and these constituted the greatest number) such an assumption seems permissible.

In view of the association made by some between the presence of accidental murmurs and assumed low arterial tension, I wish to state that the average blood pressure in these children, taken with the Riva-Rocci apparatus (narrow armlet), was 119 mm. Hg., which is one point higher than that given by Hayashi for 108 children of similar ages examined with the same instrument. In no instance was the blood pressure below 100.

The cause of these murmurs appears to be, as has been pointed out, the varying tension exerted by the heart on the overlying and adjoining lung tissue which, when diminished during the systole of the heart, permits of air entering or being sucked into previously compressed vesicles, thus giving rise to a cardiopulmonary gush in the systolic phase of the heart cycle. In one or two instances the murmur seemed prolonged into diastole.

The increase in loudness of the murmurs often when the subject is placed in the left-sided position, and the appearance of the murmur to the right of the sternum, where it had not previously existed, when the child was placed in the right lateral position, is strong support of the above premises of their causation. Likewise, the fact that if the intrapulmonary tension is increased by deep breathing and holding of the breath, the murmur often disappears entirely, is equally convincing.

The greater frequency of these murmurs in the recumbent than in the upright position is apparently due to the ascension of the heart, as indicated in many instances by the elevation of the upper border and the apex, the result of which would be the pressing aside and above of overlapping lung tissue, producing conditions favorable for the development of cardiopulmonary murmurs. These conditions are not only favorable for the development of accidental murmurs, but are also favorable for better auscultation of organic murmurs, by a greater bearing of the valve area.

I have purposely avoided mentioning and commenting on the numerous theories that have been suggested in explanation of accidental murmurs, and have merely suggested the cardiopulmonary theory as a plausible one for the murmurs of late childhood, presenting the characteristics above stated. An explanation of the cause of the auscultatory phenomena of the heart heard in these children is of far less practical importance than their recognition and the knowledge of their significance or lack of significance.

The conditions found in late childhood with regard to the area of dulness and the auscultatory findings of the heart are such as may lead to considerable confusion in their interpretation, and undoubtedly constantly do, when they are not well understood. They have frequently been supposed to mean dilatation of the left ventricle,

relative mitral insufficiency, strained ventricle, etc. A clear understanding of the conditions existing in children as to the area of dulness and auscultatory findings of normal hearts would probably avoid many such errors, because the presence of accidental murmurs (cardiopulmonary) in childhood is, I think, devoid of pathological significance.

The frequency of accidental murmurs in the children examined by Hamill and Le Boutillier[1] were practically the same as in those examined by me. The differentiation they draw, however, between late systolic pulmonary murmurs, which they incidentally refer to as an abnormal condition, and cardiopulmonary murmurs, appears to me a distinction without a difference. I consider it quite impractical to describe refined qualitative differences in murmurs, with the expectation that it will appear the same to other than the one who described them, for, after all, differentiation of systolic murmurs on this basis is not tenable. In other words, it is not practical to differentiate by the character of the murmur between accidental murmurs over the heart area, presumably dependent on different causes, nor is it practical always to differentiate between accidental and organic murmurs from the qualities of the murmur. This at once raises the question of the value of the systolic murmur in general as a diagnostic sign, whence an accurate knowledge of the normal heart becomes indispensable to a decision in children. The systolic murmur is only one of the several signs essential in the diagnosis of valvular lesions.

IMPROVED METHODS IN THE SUCCESSFUL OPERATIVE TREATMENT OF CLEFT PALATE.

By John B. Roberts, M.D.,

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The advisability of plastic operations for the repair of congenital clefts of the palate was for a long time debatable—because successful closure of the gap and a fair restoration of normal speech were unusual. The rejection of osteoplastic operations and the adoption of ingeniously constructed obturators with a movable velum were earnestly advocated by some surgeons.

After a thoughtful experience with various forms of operation and with obturators, I have come to certain definite conclusions which may be worthy of consideration. I have been led to the presentation of these views by the recent publication of articles on the

[1] Amer. Jour. Med. Sci., 1906, cxxxiii, 55.

treatment of cleft palate, which show me that my experience and practise differ from those of some other American operators. In some essential points my opinions have been radically changed within the last few years; in others, I have reached conclusive views, where previously my mind was unsettled.

The view that operations on fissures of the palate should be delayed until the child has become two, three, or four years old is erroneous. It is better to operate when the infant is only a few days old, unless there be some very grave physical debility. In that event the operation may be delayed a few weeks, but such a delay is a misfortune. The time thus occupied in building up the infant's health may be profitably employed in digital compression, applied daily to the two halves of the upper jaw. Squeezing the separated segments of the hard palate together a few times every morning and

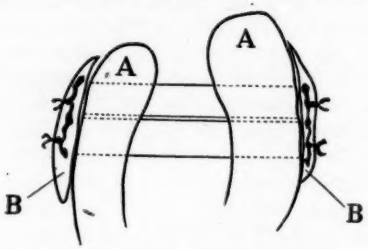

FIG. 1.—Diagram of Brophy's method of forcing and holding the two halves of the infantile cleft palate together by means of silver wires passed through the jaw above the alveolar process. By repeated pressure and gradual tightening of the wires, at the time of operation, the osseocartilaginous roof of the mouth is reconstructed. A, alveolus; B, lead plate. View from the mouth.

evening will tend to lessen the breadth of the cleft and give the surgeon a better opportunity of obtaining a bony roof to the mouth by operation.

Better than this, however, is operation a day or two after birth. My belief is that the proper course, then, will usually be to adopt the method of Brophy, who, by means of long needles, carries strong wires through the two upper maxillary bones above the level of the palate (Fig. 1). The ends of these wires are passed through holes in leaden plates, placed on the external, or buccal, surface of the bones. After the two parts of the hard palate have been forced as near together as possible, by the surgeon's fingers, the adjoining ends of wire are twisted and the bones thus held in the new position.

This procedure causes the loss of but a few drops of blood, gives rise to little or no surgical shock or pain, and has the inestimable advantage of restoring wholly or in part the normal width of the defectively united roof of the mouth. Even if the two upper maxillary bones cannot be brought absolutely together much is gained by diminishing the width of the cleft in the upper jaw. If restora-

tion of the oral roof is not done thus early the sucking and chewing of the babe and future child perhaps tend during the first years of life to increase the width of the palatal fissure. After the use of the wire tie-beams, as they may be called, for about eight weeks, muco-periosteal flaps from the oral surface of the palate may be used to close any remaining gap in the hard palate, and the soft palate may be closed by freshening and suturing its edges, which now lie comparatively close together, or by using flaps of mucocellular tissue, as in Lane's operation. In narrow clefts the soft palate may be sutured at the time the wires are introduced to bring the two halves of the bony palate together (Fig. 2).

This operation seems to me to be a most valuable addition to our resources. I believe it to be philosophically surgical, since it has for its foundation the idea that the bony elements of the

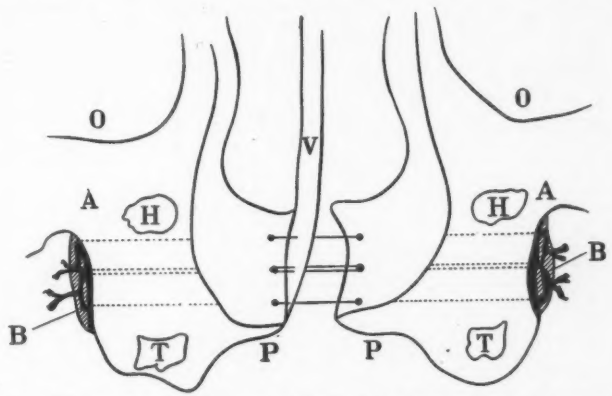

FIG. 2.—Diagram of a vertical view of Brophy's tie-beam method: A, jaw bone; P, palate; T, tooth; H, antrum; B, lead plate and wires; V, vomer; O, orbit.

normal partition between nose and mouth should be compelled to aid in the restoration of function to those two cavities.

The closing of any gap left, after all that is possible has been gained by the Brophy operation, I would usually effect by muco-periosteal and mucocellular flaps made and sutured after the manner of Lane. This method is also to be employed, without a preliminary osteoplastic procedure, in patients in whom the operative treatment has been postponed until the child is over five or six months old, and in cases in which the cleft involves only the soft palate.

One should not be tempted to operate on the harelip, if this coexist, before treating by operation the palatal deficiency. It was formerly a common practise to correct the labial deformity early in infancy, and postpone the operation on the roof of the mouth for several years. This is an error. The great improvement in the

physical appearance of the child resulting from the closure of the harelip is admitted. It is much more important, however, to close the roof of the mouth as soon after birth as possible, in order that the nasopharynx and accessory sinuses of the nose may be developed by the pressure of inspired air. The whole facial appearance of a growing child is changed by the direct and indirect influence of this conversion of a mouth breather into a nose breather. An additional result may be expected from closing the opening in the oronasal partition of the baby. It is the avoidance to a great extent at least of the catarrhal rhinitis and pharyngitis so common in cleft palate patients.

Closure of the lip does not effect these desirable improvements in the child's health and facial contour; and, if done before the palate operation, it is in a sense detrimental, because it interferes somewhat with the necessary uranoplastic manipulations by lessening the ease of approach to the operative field. The proper course, therefore, is to close the palate first and to operate upon the lip subsequently. The two operations at times may be done under the same anesthesia, or the labial operation may be delayed a couple of months.

When a cleft palate patient is over six months old it is difficult, if not impossible, to press the two separated upper jaw bones together, so as to close or diminish the intervening cleft. The cartilaginous character of the newborn baby's skeleton is lessened at that age by increasing deposition of inorganic salts. The exact age at which the bones become too rigid for successful displacement varies. In the early weeks of life they may be bent into the desired position without fracture occurring; later they may sustain a green-stick fracture through the body of the jaw above the malleolus. In some cases it is necessary to divide the two upper maxillary bones at this point by a horizontal section with a saw.

This increasing difficulty of forcing the bones toward the median line, so as to hold them together with wire tie-beams, is the chief reason for early operation. Brophy maintains that in most cases of cleft hard palate there is no real deficiency in the amount of osseo-cartilaginous material to form the roof of the mouth; but that the two halves have simply failed to unite and are spread apart. Hence the value of his method of forcing the palatal processes together and holding them in apposition until union is obtained. The importance of giving the muscles of phonation and the bones of the mouth and nose an early chance to develop and perform their physiological duty will be recognized by all. Delayed operative reconstruction of the palate means progressive atrophy of muscles and other tissues from disuse, and the development of abnormal relations and activities of the parts.

When the palatal segments cannot be brought together even after sawing the bodies of the bones, or when the true physiological time

for this operation has passed, the surgeon should close the gap in the bony palate by means of flaps of mucoperiosteum cut and sutured as suggested by Lane (Fig. 3). I have had far better success by this method than by displacing two flaps toward the middle line, as is done in the Langenbeck and Fergusson operations.

Lane raises a large mucoperiosteal flap from the side of the fissure, where there is the larger expanse of palatal tissue. This flap is cut with its free convex border at, or actually upon, the alveolar process, and is left attached at the margin of the congenital cleft. On the opposite side a flap is raised, which is cut loose from the bone at the margin of the cleft and remains attached, for its blood supply, to the bone near the alveolus. The first flap is then turned over, laid across the fissure in the bone, and tucked under the flap raised on the opposite side of the palate. It is sutured in this everted position by two rows of delicate silk sutures inserted

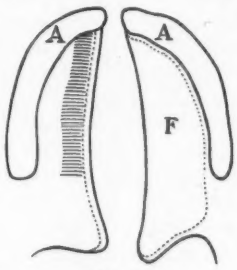

FIG. 3

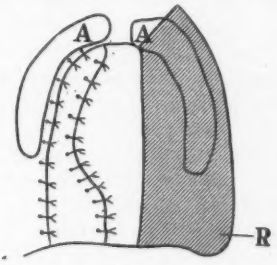

FIG. 4

FIG. 3.—Diagram of the roof of the mouth, showing incisions by Lane's method. A, alveolus; F, flap which is to be everted and tucked under the raised flap on the opposite side. The shaded portion indicates where the raised flap is to be separated from the hard palate.

FIG. 4.—Diagram showing the appearance after the flaps in Fig. 3 have been sutured: A, alveolus; R, raw surface left after the flap has been everted.

with very small curved needles (Fig. 4). The raw surface of the first flap faces the tongue and subsequently becomes cicatrized with a pseudomucous membrane.

This method of utilizing the flaps has the advantage of covering the gap without much tension of the tissues. In addition the secretions from the nose have slight access to the suture lines and therefore the suture punctures are not likely to become infected. The raw surface of the large flap is constantly cleaned by the patient's tongue (Fig. 5).

When the operation is done before the child has developed molar teeth the first flap may be made of extreme width by cutting it from the top and outer side of the alveolar process as well as from the surface of the palate. It may even extend upon the cheek. I know of no other method of uranoplasty which makes available such an extent of well-nourished tissue.

About eight years ago I endeavored to close a palatal cleft by everting a mucoperiosteal flap from each side of the fissure and suturing them in the middle line. I did not know of Lane's method at that time. The cicatricial contraction of the periosteal surfaces made the flaps curl up toward the mouth and caused a failure, after I had thought successful closure of the gap was accomplished. Lane has solved this difficulty and made the plastic operation generally successful by everting only one flap and tucking its free edge under a raised flap on the opposite side of the congenital fissure. When I

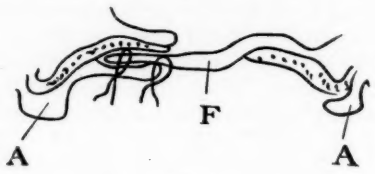

FIG. 5

FIG. 5.—Diagram to show in section the relation of the flaps after suturing in Lane's operation: A, alveolus; F, large flap which has been everted and tucked under small flap.

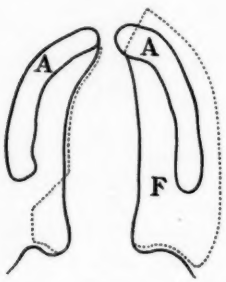

FIG. 6

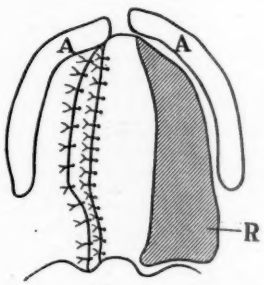

FIG. 7

FIG. 6.—Diagram to show incisions for flaps in Lane's method when the cleft is very wide, and the large flap must include the mucous membrane over the alveolus. The posterior part of the incision on the left side of the diagram is on the nasal surface.

FIG. 7.—Diagram to show appearance when in Fig. 6 the flaps have been sutured

used the method of Langenbeck and Fergusson, I always entered upon the treatment of cleft palate with misgivings. Now, on the other hand, I am always glad to see such patients, whether they be poor or well-to-do, for I feel so much more sure of obtaining a good result.

It not infrequently happens that the entire palate cannot be repaired at the first operation; but subsequent minor operations, so common in all plastic work, finally complete the reconstruction (Figs. 6 and 7). With the early closure of a cleft palate made practically

always possible and the operative treatment of harelip so satisfactory as it has now become, in skilled hands, surgery holds out to the unhappy parents of the deformed little ones a great deal of comfort.

I formerly used obturators, or artificial palates, occasionally, because of my fear of operative treatment being less satisfactory. These cannot be worn until the child has attained nearly the age of adolescence. Then the secondary atrophy of the nasopharynx and facial skeleton have become established and the speech defects confirmed. Mechanical appliances are, therefore, to be usually rejected in the consideration of the treatment of congenital clefts of the palate. They may at times be employed when the patient has been allowed to grow up without operative treatment in infancy; but they are even then probably a poor makeshift for reconstructive treatment by operation.

In all cases of this congenital anomaly systematic instruction in respiration and speech should be begun immediately after the palate has been repaired by operation. The child must dilate, as it were, the nasopharynx and accessory sinuses of the nose, and train the muscles of phonation, as well as the corresponding brain centres, to do their full physiological duty.

In conclusion, I state my opinions as follows: Cleft palate should be operated upon as soon as possible after birth. Accompanying harelip should not be treated until after the palate operation. When the operation is done during the first six months of life, Brophy's tie-beam method should usually be adopted.

After six months of age, the Lane flap method should generally be employed. At times it may be needed as a supplement to Brophy's method in younger patients. Brophy's method for these cases by means of silver-tension sutures and coaptation sutures with lead splints, or plates, applied to the inferior surface of palate flaps, is also very valuable.

Mechanical appliances to close the fissure are inferior to operative treatment, which has a low necessary mortality.

Instruction in speech is a necessary adjuvant for satisfactory results.

OBSTETRIC PARALYSIS.

By William Norton Bullard, M.D.,

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No better illustration of the rapid advance of medical knowledge and treatment within the last quarter of a century can be found than that offered by the history of obstetric paralysis. It was first brought

to the notice of the medical profession by Duchenne in 1872. Yet even in 1886, Thorburn[1] could find but five articles on the subject. Since 1900, however, a certain number of cases have been described in the literature and a few articles have been written both on the etiology and on the surgical treatment. Although the condition appears to be a comparatively simple one pathologically, it is only of late that it has been understood. Many plausible theories have been formed, but it is only within the last few years that the visible pathological proof has been found and the evidence from experiments and dissections has been obtained.

For practical purposes we may divide obstetric paralysis into three forms: (1) The upper-arm type; (2) the lower-arm type; and (3) the two preceding combined, paralysis of the whole extremity. The lower-arm type is rare. Dr. Thomas[2] has recently described and discussed the cases of this character.

The common form of obstetric paralysis is the upper-arm type, corresponding in a general way pathologically to Erb's paralysis in the adult. This includes the large majority of cases of obstetric paralysis which are commonly seen, and I shall restrict myself to the consideration of this form. It was suggested by Erb that this type of paralysis is due to inhibition of conduction, whether by pressure, section, or destruction of the fifth and sixth cervical nerve roots, and he determined that faradization of these nerve roots irritated or caused contractions of the muscles paralyzed. Later, within the last ten years, operations performed on the brachial plexus in cases of Erb's paralysis in adults have confirmed the fact that these nerve roots are injured in this form of paralysis, and conversely have tended to prove that the injury of these nerve roots is the cause of this paralysis. The cause of the lower-arm type is injury of the seventh and eighth cervical and first dorsal nerve roots; when the whole limb is totally paralyzed, all the nerves, fifth, sixth, seventh, and eighth cervical and first dorsal, are affected.

Although the position of the lesion in obstetric paralysis had been assumed as a fact from the time of Duchenne, the cause of this lesion long remained obscure. Nearly all the earlier writers attributed it to pressure. Duchenne, followed by others, believed that direct pressure by the forceps on the nerves going to form the brachial plexus was the cause. Others asserted that it was due to pressure on the brachial plexus between the clavicle and one of the transverse processes: others that it was caused by pressure or squeezing between the clavicle and first rib. From personal experiments it is in my mind exceedingly doubtful if these conditions are anatomical possibilities in normally built babies. I should not be willing to admit such a cause without absolute proof. It is, however, possible that in cases of fracture of the clavicle, or other fracture,

[1] Med. Chron., Manchester, 1885–1886, iii, 446.
[2] Boston Med. and Surg. Jour., October 19, 1905.

some pressure on the brachial plexus may be produced which may cause similar or analogous symptoms to those of ordinary obstetric paralysis. Thorburn mentions this class of cases merely to exclude them from consideration under this title.

Setting aside the theories of direct pressure on that portion of the brachial plexus capable of producing these forms of paralysis, we find certain other theories advocated to explain the clinical conditions which later have proved inadequate and have been discarded. In 1892, Chauncey R. Burr[3] attempted to explain these cases as forms of anterior poliomyelitis, a theory which at the time had some plausibility and which in the absence of the objective evidence of the nerve lesion might be hard to disprove.

Carter,[4] in 1893, published an excellent article on this subject. In France experiments were made on the rabbit and on the cadaver by Fieux[5] and these with accounts of cases were reported by him in 1897.

The true condition in many if not all of these cases was made evident (1) by conditions found in traumatic cases of Erb's paralysis in the adult, (2) by experiment on the cadaver and on animals. The first case in which the condition existing in a case of obstetric paralysis was seen was that of Eversmann[6] in 1903. In this case there was found a hard, tumor-like thickening, 0.5 to 0.75 cm. long, at the junction of the fifth and sixth cervical nerves, evidently a callus following a primary injury with laceration of the nerves.

It has now, however, been shown by a number of cases that the injury is due to stretching of the fifth and sixth cervical nerves in the neck. These nerves may be simply stretched without loss of continuity or they may be ravelled out, some fibers being torn apart and some still holding, or they may be wholly torn asunder. The second is probably the most common condition. One nerve may be wholly torn and others partially so. Personally I have had occasion to see this condition in one case.

The history of the various theories which have been held in regard to the etiology and pathology of obstetric paralysis has been so thoroughly abstracted and discussed by Stransky[7] (1902) that further consideration of this subject here is not advisable. Anyone specially interested should consult his most excellent and valuable article.

ETIOLOGY. The exact causation of obstetric paralysis, the method in which the pathological condition is produced at birth, is still not perfectly clear. We know that at least in the very large majority of cases the nerves are torn or ravelled out, but the exact process by which this is done is not settled. It seems certain that it is due

[3] Boston Med. and Surg. Jour., 1892, cxxvii, 235.
[4] Ibid., 1893, cxxviii, 434.
[5] Ann. de gynec. et d'obstetrique, 1897, xlvii, 53.
[6] Arch. f. Gynäk., 1903, lxviii, 143.
[7] Centralblatt f. d. Grenzgebeite d. Med. u. Chir., 1902.

to traction powerfully exerted and favored by a firm resistance or fulcrum against which the pull is made. The injury to the nerves is undoubtedly favored by placing them on the stretch through the position of the head. A traction on the head in the axis of the body is less injurious than when the traction is made obliquely so that the head is inclined to one side while the traction is made. Rotation of the head to the opposite side also stretches the nerves and traction made while the head is rotated, particularly when it is also inclined toward the shoulder opposite the stretched nerves, strongly favors injury. In order that the full force of the pull should be effective against the nerves, it is necessary that there should be firm resistance. In the case of head presentations this may be produced by the fixation of the shoulder or shoulders; in the case of breech presentations by the resistance of the head.

Other factors enter into consideration also. It is extremely probable that forced lowering of the shoulder girdle acts unfavorably to the resistance of the nerves and favors this injury. The catching or fixation of the tip of the shoulder produces this lowering, and this we know must often occur. In cases of traumatic Erb's paralysis in the adult the causation is frequently a severe blow upon the shoulder, causing its sudden forced descent.

Asphyxia has been considered as an important factor in the production of this condition. When the patient is asphyxiated the muscles become relaxed, their resistance is removed, and the nerves, no longer having their support, are more easily torn.

STATISTICS. In order to determine practically, as far as possible, the mechanism or causation of the injuries causing obstetric paralysis, I have investigated a considerable number of cases from the Department of Nervous Diseases at the Children's Hospital, Boston. A request was sent to the attendant physicians asking for an account of the delivery and labor. Through the kindness of many of these gentlemen, I have received replies which may be summed up as follows:

Statements from Physicians. I have 43 cases in which the report of the attending physician has been obtained. The character of the labor was described as long, tedious, or difficult in 20 cases; in 6 cases it was noted as normal, and in 4 cases as easy; in 2 cases of the latter as "unusually easy." In 13 cases there was no report as to the character of the labor. It was not possible to distinguish between the protracted labors and those which presented difficulties and obstacles and were classed as "difficult." The two conditions do not coincide, but they are apt to occur together; especially is the difficult labor apt to be prolonged.

The delivery is described as difficult in 15 (very difficult in 7), easy in 1, normal in 6, and is not reported in 21 cases. Forceps were used in 28 cases: in 8 high forceps; in 1 it was noted "medium"; in 2 low. Ether was used in 12 cases.

The head presented in 40 cases, the breech in 3. This would seem, in comparison with statistics obtained from the literature, to be an unusually small proportion of breech presentations.

As to the position of the head, in one case it was noted that the occiput presented. O. L. A., or first position, occurred in 18 cases; O. R. A. in 1 case; the occiput anterior was noted in 1 case, the occiput posterior in 2 cases; O. D. P. in 2, and a face presentation in 2. In 13 cases the presentation is not stated.

In 18 cases it was especially noted that the shoulders were held or offered resistance to extraction, and this fact has been considered by the reporters as unusual and of great importance. On the other hand it was expressly recorded in 5 cases that the shoulders were not held. In regard to traction, it was recorded as used on the neck in 2 cases, on the head in 2 cases, and on the shoulder in 1 case. In 5 cases there was pressure in the axilla by the finger or otherwise. In these cases it is fair to suppose that traction is only mentioned when considerable force was used, at least more than the ordinary amount.

It was mentioned in regard to the arms that in 5 cases they were brought down with difficulty. In 1 case the arm was stated to have undergone great pressure between the body and the pubes. In 2 cases there was no traction. The position of the arms was not mentioned except in 2 cases, in neither of which were they above the head.

These are the results which are obtained from the statements of the attending physicians and are our most reliable data.

From the patients themselves we have in many cases obtained good histories. In addition to the cases in which we have physicians' reports we have 135, making a total of 178.

Statements from Patients. Duration of labor, six hours or under, 12 cases; between six and twelve hours, 8; between twelve and twenty-four hours, 17; between twenty-four and forty-eight hours, 5; forty-eight hours or more, 9 cases.

Labor, severe, difficult, 79 (prolonged, 2); mother died at birth, of nephritis, 1; easy, 1; short, 1; not difficult, 1; normal, 4; and dry, 1.

Presentation. Head, 55; breech, 5; feet, 5; transverse, 3; arm, 2.

Forceps (including 3 on the after-coming head), 93; no instruments, 20.

Anesthetics. Ether, 27; chloroform, 3; no ether, 9. Asphyxia, 42; no asphyxia, 19. Shoulders delayed, 19; head large, 1; caught, 1; body delayed in breech presentation, 1. Arms over head, 2; arms caught, 4.

Injuries. Fracture of clavicle, 5; fracture of arm (humerus), 2; dislocation of shoulder, 4.

As to the limb affected the statistics are: Right upper extremity (breech 2), 92; left upper extremity (breech 1), 72; both, 2; not reported, 11; one case omitted as not obstetric paralysis, 1.

It has been suggested that in head presentations the paralyzed arm corresponded to the shoulder which was held under the pubes. This shoulder being fixed, the strain came upon the nerves on this side and the corresponding limb was injured. Hence in the O. L. A. position in which the right shoulder is held under the pubes the right upper extremity should be the one paralyzed. This theory is not confirmed by my observations, as out of the 17 cases of O. L. A., in 8 the right upper extremity was the one involved, and in 9 it was the left upper extremity.

Clinical Conditions. The clinical conditions vary in different cases of obstetric paralysis, according as we have the upper-arm type (Figs. 1, 2 and 3), the lower-arm type, or the type which involves the whole extremity. I shall consider in this paper only the upper-arm type. In the larger number of cases of this character we find involved the deltoid, biceps, brachialis anticus, the supinator longus and perhaps the brevis, the infraspinatus and supraspinatus, and serratus magnus. Occasionally there are other muscles involved, as the rhomboids, the subscapular, and probably the coracobrachialis and subclavius.

If the other roots have been wholly or partially involved there is more or less affection of other muscles of the limb, involving the movements of the arm, forearm, or hand, and the case approaches the third type. The clinical results of involvement of these muscles can be more or less logically anticipated.

Clinically we find the following conditions:

In the early stages the upper extremity hangs limp, extended by the side, and the whole limb is internally rotated. In typical cases the grasp is unimpaired in this type, and the wrist is not affected. The forearm cannot be supinated beyond the median line. Flexion of the forearm on the arm is weak and poor, not wholly absent, extension not affected. The arm cannot be elevated at the shoulder nor can it be rotated outward; inward rotation is impaired, inasmuch as the limb is held more or less fixed in the position of internal rotation. Passive movements are now perfectly free.

The anatomical causes of the typical position of the upper extremity and of its inability to perform certain movements in obstetric paralysis of the upper-arm type are very interesting.

Inasmuch as the extremity assumes at once on the outset of the paralysis its typical position, it is plain that this must be due to the uncontrolled action of the unparalyzed muscles. The three principal elements of the typical position are the internal rotation of the arm and forearm, the extension of the forearm on the arm, and the hanging of the arm due to inability to raise it at the shoulder.

(*a*) The internal rotation of the arm is due in most cases to the action of the pectoralis major and the subscapularis. Perhaps it is more accurate to say that the pectoralis major adducts the arm and brings it forward on to the breast while the subscapular rotates

FIGS. 1, 2 and 3.—Obstetric paralysis, upper arm type; characteristic position of the arm

it. The latissimus dorsi and teres major assist in the internal rotation of the arm.

(*b*) The pronation of the forearm and hand is caused partially by the internal rotation of the arm. It is also caused undoubtedly by paralysis of the supinator brevis, and especially by the paralysis of the biceps.

(*c*) The extension of the forearm on the arm is due to the paralysis or weakness of the flexors of the forearm in the arm, the biceps, brachialis anticus, and coracobrachialis.

(*d*) The hanging of the upper extremity from the shoulder is due chiefly to the paralysis of the deltoid. The weight of the limb itself causes this when its support is removed.

If we examine more closely into the involvement of the muscles in the upper-arm type of obstetric paralysis we shall be in a better position to understand, at least in part, the conditions which are found.

We shall consider the muscles in turn. (The nerve supply is given in parentheses after each muscle.)

I. *Serratus Magnus.* This is usually involved. It has been stated by some writers that it is never involved, but this I believe to be a mistake. (Posterior thoracic nerve.) Angel-winged paralysis.

II. *Subscapularis.* It is practically impossible clinically to state in most cases whether this muscle is involved or not. In many cases it seems to be normal. (Subscapular.) Inasmuch as the internal rotation of the arm is presumably in most cases caused by this muscle, the clinical evidence is in favor of its not being weakened or paralyzed.

III. *Supraspinatus* and

IV. *Infraspinatus.* These muscles are usually involved and often markedly atrophied. In the typical cases they are involved and atrophied. (Suprascapular.)

V. *Teres Minor* and

VI. *Teres Major.* The teres minor is quite certainly usually involved, although this is not always apparent to the eye. (Circumflex.) There is more doubt in regard to the teres major, but it is probably usually affected. (Lower subscapular.)

VII. *Deltoid,*

VIII. *Biceps,*

IX. *Brachialis Anticus.* These three muscles are always involved. The deltoid is the most affected, as a rule, of any muscle, and is in all typical cases atrophied. The biceps and brachialis anticus are always weakened and are atrophied in all severe cases.

X. It is often said that the *coracobrachialis* is not involved. This is somewhat difficult to prove. (Musculocutaneous.)

XI. *Triceps* not involved. (Musculospiral.)

XII. and XIII. *Supinator longus* is involved in all typical cases —usually much involved. (Musculospiral.) The *supinator brevis* is said to be involved in many cases. (Posterior interosseous.)

XIV. *Subclavius.* It has been said that the subclavius is sometimes involved. (Cord of fifth and sixth.)

XV. *Pectoralis Major.* In large part not involved. In some cases the upper portion is distinctly atrophied. (Anterior thoracic.)

XVI. *Pectoralis Minor.* No clinical evidence of involvement. (Anterior thoracic.)

SUMMARY. Typically involved are the deltoid, biceps, brachialis anticus, supinator longus, supraspinatus and infraspinatus, serratus magnus. Probably usually or frequently involved in addition are the teres minor, coracobrachialis, and supinator brevis. The subclavius is probably sometimes involved. The upper portion of the pectoralis major is sometimes involved. The subscapular is probably not often affected. The trapezius is apparently often weakened.

The cause of the inability to perform certain movements in this affection is the paralysis of the muscles by which these movements are performed. It is a task of considerable difficulty to determine what muscles are involved in each case.

The *general rules* are as follows: The inability to raise the arm to the level of the shoulder is due in large part to the paralysis of the deltoid and the supraspinatus. The serratus magnus and trapezius aid in performing this movement in the healthy person.

The inability to elevate the arm from the level of the shoulder to the full height is due chiefly to paralysis of the serratus magnus. In the healthy person the deltoid and trapezius assist in this movement.

The inability to rotate the arm externally is due to the paralysis of the infraspinatus and teres minor. The posterior portion of the deltoid helps in the healthy to perform this movement.

The inability to rotate the arm internally is due to the fact that the internal rotators are already fully contracted.

The weakness and inability to flex the forearm strongly is due to the weakness or paralysis of the biceps, brachialis anticus, coracobrachialis, and supinator longus.

The inability to supinate the forearm is due in part to the position of the arm and in part to weakness of the biceps and the supinator brevis.

The inability to extend the forearm fully on the arm which is present in many old cases is due sometimes to actual atrophy and malformation of the bones, and at others apparently to a contraction of the capsule of the joint, especially the anterior portion.

As the paralysis continues new conditions arise. On examination of the older cases we ordinarily find an atrophy of the scapular muscles well marked, sometimes a rotation of the scapula or a standing off of its internal border from the ribs, which might be caused by weakness of the trapezius or of the serratus

magnus. There is usually marked atrophy of the deltoid and some atrophy of the whole extremity, most apparent in the arm, somewhat in the forearm, while the intrinsic muscles of the hand are little or not at all affected.

The atrophy of the limb is, in the older cases, not confined solely to the muscles, but the bones themselves are affected and the whole limb may thus be smaller than the corresponding one. We may find at the shoulder a loose joint, though this is less extreme than in some cases of anterior poliomyelitis. I would here call attention to the fact that the atrophy and paralysis of the arm muscles is less complete, as a rule, than in the old cases of anterior poliomyelitis. This may be due to the fact that in the laceration and ravelling of the nerve cords some fibers are left unhurt or are not totally destroyed.

In these cases other conditions develop or appear. It is common to find evidences of adhesions between the scapula and the structures of or around the shoulder-joint, so that in partial passive elevation of the arm the scapula is moved, and as the arm becomes elevated above the level of the shoulder the scapula is drawn into the axilla. Inability to produce absolute extension of the forearm occurs in many cases. Its cause will be discussed later.

Passive supination of the forearm is sometimes impossible, apparently on account of adhesions.

Atrophy and Malformation of Bones. In addition to the muscular atrophy we find evidence of atrophy or non-development of the bones. The limb may be actually shortened in comparison with the healthy one.

Shoulder. Displacements of the head of the humerus are not rare. The head of the humerus is usually displaced anteriorly. There is an anterior subluxation. It may, however, be displaced posteriorly —posterior subluxation.

These displacements are due apparently to the contractions of the unparalyzed muscles and possibly of some of the tissues surrounding the joint. There is no evidence of any contracture of the paralyzed muscles.

The paralysis is always flaccid. The capsular ligament surrounding the joint is undoubtedly stretched.

I had long supposed the anterior subluxation to be due chiefly to the contraction of the pectoralis major, the upper portion of which can be felt hard and tense, holding the arm fixed in internal rotation. I am inclined to believe now, however, that the subscapular plays an important part in this connection.

The cause of the posterior subluxation is more doubtful. The paralysis of the supraspinatus is undoubtedly the most important factor. The latissimus dorsi and the sternocostal portion of the pectoralis major by their contraction tend to separate the head of the

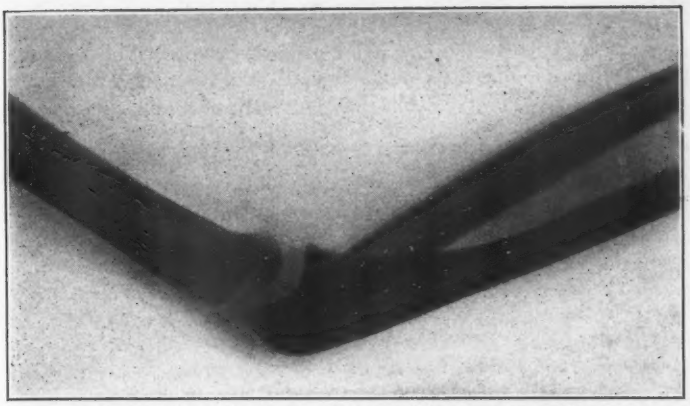

FIG. 4—Elbow-joint, showing backward dislocation of the radius.

FIG. 5.—Elbow-joint, showing lack of development of the olecranon and impairment of extension by bony contact.

FIG. 6.—Lateral displacement of the elbow-joint.

humerus from its socket, and if unopposed may cause subluxation. They are opposed by the coracobrachialis and the long head of the triceps.

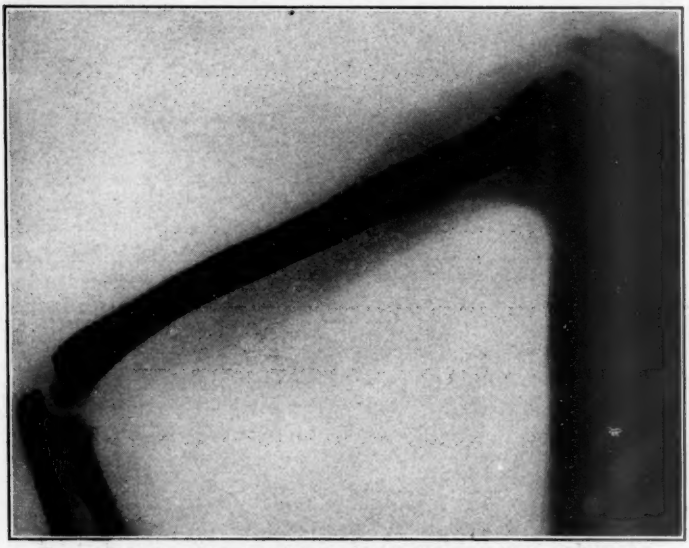

FIG. 7.—Posterior subluxation of the head of the humerus, with marked atrophy of the bones of the arm and forearm.

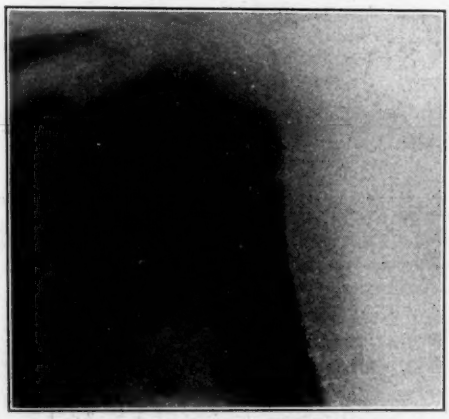

FIG. 8.—Anterior subluxation of the humerus.

Stone (1900) states that backward dislocation of the humerus is due to the stretching of the posterior portion of the capsule, which

is weaker than the anterior portion, and that this stretching is the result of the strong internal rotation of the humerus, aided by the backward and downward pull of the latissimus dorsi.

Elbow. It is usually the case that extension of the forearm on the arm is impaired. Full extension, either active or passive, is not possible, resistance being encountered toward the end of extension.

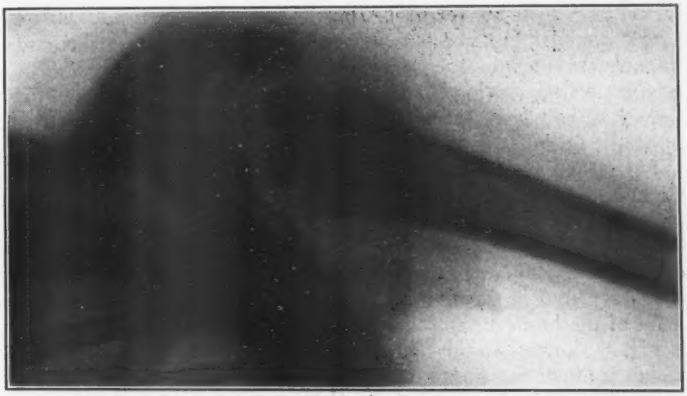

FIG. 9.—Posterior subluxation and atrophy of the head of the humerus.

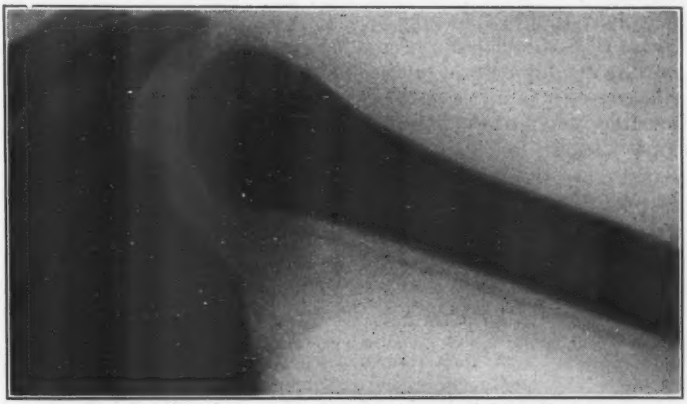

FIG. 10.—Posterior subluxation of the humerus and dropping of the humerus.

The forearm cannot be extended fully in the axis of the arm, but remains at an obtuse angle of 170 to 175 degrees.

This may be often due to the contraction of ligaments or of the tissues surrounding the joints, but it is at times due to atrophy and malformation of the bones themselves, as may be seen in the accompanying *x*-ray prints.

In Fig. 4 there is a backward dislocation of the head of the radius, and as a result of this the head is much elongated and thinned. The impairment of motion occurs less sharply than in Fig. 5.

Fig. 5. The limitation here is due to the lack of development of the olecranon, which does not extend backward and upward to the normal amount. The result is that when the elbow is extended the tip of the olecranon impinges on the articular surface of the humerus instead of sliding up behind its lower end, and thus by actual bony contact prevents full extension. In this case the actual impairment of movement appears increased to the observer on account of the curving forward of the lower end of the shaft of the humerus, which in addition to the real impairment produces an apparent flexion.

Fig. 6 is another excellent radiogram of an elbow in this affection. There is some lateral dislocation and the bones hitch on extension.

Fig. 7 is a radiogram showing both the shoulder-joint and the elbow-joint. There is marked atrophy of the bones of the upper extremity, and in this case there was a posterior subluxation of the head of the humerus.

Fig. 8 shows anterior subluxation of the head of the humerus, which is about the normal size and is to be compared with

Fig. 9, which shows marked atrophy of the head of the humerus in a case with posterior subluxation, and retarded development of the epiphysis.

Fig. 10 is a radiogram of another case of posterior subluxation, showing the dropping of the head of the humerus from the scapula on account of paralysis of the deltoid and stretching of the capsule from the weight of the limb. This is from the same patient whose elbow is shown in Fig. 5.

TACTILE AMNESIA.

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Not infrequently patients suffering from hemiplegia are unable to recognize by touch objects in the paralyzed hand. This must occur if there is complete insensibility to all forms of sensory stimuli. But it also occurs when there is only partial insensibility, when only certain kinds of sensations are unperceived. Mere tactile anesthesia —that is, the inability to feel contact on the skin without pressure or at least with no more pressure than is made by a wisp of cotton— does not prevent the recognition of objects. When the anesthesia

affects the underlying tissues so that deep pressure is not felt, the patient not only does not know what he has in his hand, but does not know that he is grasping anything. More important, then, than light touch in the recognition of objects is the ability to know the position of the fingers, to differentiate weight, to locate the point touched, and to recognize the number of points of contact. Failure in these regards, even if mere touch sensibility is preserved, leads to true astereognosis. In healthy men objects are distinguished much more accurately by handling them than by contact with any other part of the body. Some objects (apart from recognition by taste) can be recognized by contact with the lips, tongue, and mucous membrane of the cheeks. The ability to recognize objects in contact with the feet is almost *nil*. This is probably largely owing to the fact that throughout life no attention is given to educating the sensibility of the feet and partly to the lack of prehensile power in the toes. Armless men who have learned to use their feet more or less well as their hands have a greatly developed power of recognition of objects by them. Persons who have been hemiplegic from birth or early childhood are sometimes astereognostic in the palsied arm from lack of training.

These few preliminary words about astereognosis are necessary because it is often confused with tactile amnesia. In the latter sensibility to all forms of stimuli is preserved, but the patient, though knowing he has something in his hand, yet cannot recognize what it is. It is not that he cannot, though knowing what the object is, recall its name (tactile aphasia), but he does not know its nature or uses, knows nothing about it. Of course, the recognition of an object is a psychical process. A great number of sensations from the skin and underlying structures, muscles, and joints are combined and form the perception of a key, an apple, or whatever the object may be. Though the judgment is psychical there must be stored, somewhere in the cortex, memories of passed tactile sensations of other keys, apples, etc. Disease destroying this part of the cortex or cutting it off would lead to tactile amnesia. The location of this centre is yet not clearly and definitely known, but it probably is in either the posterior part of the parietal lobe or the anterior part of the convex surface of the occipital lobe. The frequency of the association of the symptom with word blindness and mind blindness makes it probable that the centre is near the higher visual centre. It cannot be identical with the centre for common sensation, because tactile sensibility is not affected. The frequent occurrence of the symptom with mixed sensory aphasia due to a unilateral lesion would indicate that the centre is unilateral. It must be posterior to the fissure of Rolando. The symptom never occurs if the area of disease involves only the prefrontal lobe. I have never seen it in pure motor aphasia, in uncomplicated left-sided hemiplegia, nor in right-sided hemiplegia unless there was also a greater or less degree of word blindness or

object blindness or some type of sensory aphasia. It is frequent in pure mind blindness and in mind blindness occurring as an early symptom of dementia caused by diffuse organic brain disease. There may, however, be complete mind blindness, an absolute inability to recognize any object by sight, without any tactile amnesia.

In differentiating it from astereognosis it must be remembered that there is no disturbance of primary sensibility and that both sides are affected. I have never seen it as an entirely isolated symptom and do not know whether it occurs. It is sometimes an early or late symptom of organic dementia. Its presence or absence cannot of course be determined in severe cases of total or of mixed sensory aphasia, because it is impossible to make such patients understand what they are to do when an object is put in the hand. The only patients suitable for examination are those in whom the aphasia is partial or in whom recovery has gone far enough for the patients to understand short and simple commands and to use language enough to show whether they know what they are grasping. Nothing can be judged from the patient's general conduct whether the symptom is present or not, because vision helps him in all he does. It can only be discovered by examination.

CASE I.—*Complete tactile amnesia associated with sensory aphasia, hemiplegia, word blindness, and partial object blindness.*

J. M., seventy years old, was admitted to the hospital in December, 1902, with right hemiplegia and jargon speech. His previous history could not be obtained, but he must have been ill quite a long time, because the paralyzed arm was contractured and his gait was that of an old hemiplegic. Spontaneous speech, that is, speech as a method of expressing ideas arising within his mind and not merely words recalled reflexly in response to external stimuli, was an unintelligible jargon. There was not complete word deafness. He understood and obeyed short and simple verbal commands such as "stand up," "sit down," "walk," "stand still," but failed to obey any order in the least complicated. His difficulty seemed to be not so much in understanding single words as in carrying the first words of a long sentence in consciousness until the last were spoken. Words made only a momentary impression on him. He understood gestures and pantomime fairly well. By the combined use of spoken words, gesture, and pantomime I was able to make him understand he was to tell me the names of objects shown him and put in his hands. He named at sight a box, spoon, fifty-cent piece, ten-cent piece, watch, book, penholder, candle, and scissors. He could not name and gave no evidence of recognizing a fork, cigar, key, or knife. He failed to recognize any object put in either hand. He did not understand written or printed words and could not even write his name. His condition remained unchanged for two months, when he died of chronic Bright's disease.

CASE II.—*Transitory hemiplegia and permanent jargon aphasia with partial tactile amnesia.*

J. C., seventy-six years old, was admitted to the hospital in January, 1906. Two and one-half years before he had had a stroke, causing transitory difficulty in speech. The day before admission he fell unconscious and so remained a few minutes. When consciousness returned speech was so mixed that he could not be understood and he was palsied on the right side On admission speech was so mixed that it was impossible to understand him. He was not entirely word deaf because he obeyed simple verbal commands, but he failed to obey any complicated order. There was no hemiplegia. Three days later he had improved a great deal. He wrote his own name, but nothing else. (He had been taught to read and write.) He looked blankly at written and printed words and made no attempt to obey written orders. He named at sight most numbers below 100, but failed on all larger ones. He recognized and named all the letters except U. He copied a few short words, but soon became confused and ceased to make any further effort. He did not understand the meaning of the words he copied. Spontaneous speech had improved very much. He could carry on a simple conversation for a few minutes, but soon became mentally tired and confused and then his speech became very mixed. He recognized and named at sight almost all the common objects shown him. Some objects put in either hand he recognized and named; some he recognized, as was proved by his description of them, but could not name (tactile aphasia); others he did not recognize. Some objects recognized by touch were not recognized by sight, and vice versa. There was no anesthesia of any kind in either hand. When he was discharged several weeks later spontaneous speech was quite good, but he still became confused if he talked for a long time. His disability in recognizing objects by touch and his inability to read and write remained unchanged.

CASE III is very complicated because in the paralyzed hand there was sufficient sensory disturbance to produce astereognosis, while in the left, with normal sensibility, the patient was able to recognize and name some objects but not others—partial tactile amnesia.

C. D., forty-five years old, was admitted to the hospital in April, 1905. Two months before admission he suddenly became confused, mixed in speech, and, in the course of a few hours, lost power in the right arm and leg. He had a right-sided hemiplegia. He could walk, but dragged the right leg, and the right arm was contractured. There was slight palsy of the lower right face. He had marked disturbance of spontaneous speech. On beginning to talk he did well, but soon tired, became confused, and then speech was unintelligible. He understood and obeyed simple verbal commands and answered simple questions by simple words. He became much mixed on attempting to use long sentences in talking. He recognized

and named most objects at sight; a few he described by a paraphrase or a not strictly accurate name, that is, a teaspoon was a "thing to eat with" and a cork was a "stopper." He recognized by sight all the letters and could read aloud and understand the meaning of short words. He could copy and sometimes understand words he copied. He recognized numbers of not more than two figures. He could write his signature C. B. Blank, but not his first name, Charles. He could write most letters at dictation, but no words. He could not recognize any object put in the right hand. Though the right arm was palsied, there was enough power in it to grasp and "actively" feel objects. Sensibility to touch was preserved, but though he located a single point of contact fairly well on the right hand he could not distinguish whether he was touched in one, two, or three places simultaneously unless they were very wide apart. When touched in several places at once he usually located one fairly well, but apparently had no knowledge of the others. He knew in a way, but not accurately, the position in which the fingers of the right hand were passively put, because he could put the fingers of the left hand in about the same attitude. On the left hand there was no disturbance of sensibility of any kind. In it he recognized a few objects, but failed entirely to recognize many.

CASE IV.—*Slight hemiplegia, mixed sensory aphasia, partial object blindness, and partial tactile amnesia.*

S. B., fifty years old, was admitted to the hospital in April, 1904. He had an old right-sided hemiplegia involving the face. He could walk a little and move the right arm slightly, but not use it for any purpose. On admission his speech was such a jargon that it could not be understood, and he obeyed no verbal commands. By the third day he had improved enough to understand and obey simple commands. He understood that he was to tell me what the things were I showed him and put in his hands. At sight he recognized and named a watch, handkerchief, one-cent and five-cent pieces, two and five-dollar bills (as money, but not the denomination), a spoon, a cigar, bunch of keys, and a cup. Many other common objects he did not recognize. By touch in the right hand he recognized and named a penknife, key, and watch, but nothing else. In the left hand he recognized nothing. If he handled and looked at an object he did not recognize and at the same time was told its name he did not recognize the name. Speech improved a great deal, but his visual and tactile disturbance continued until death, which occurred some weeks later from uremia.

CASE V.—*Transient right hemiplegia, aphasia, and tactile amnesia.*

W. C., sixty years old, was admitted to the hospital in August, 1904. On January 14, 1904, he awoke paralyzed on the right side and with inarticulate speech. He improved, but the day before admission speech again became affected. He had never been taught to read and write. The lower right face was slightly palsied. At

the beginning of the examination he answered questions without difficulty, but soon tired mentally and became confused and misused words. There was no disturbance of sensation. He recognized and named almost all objects shown him, but could not recognize or name any object put in either hand. In a few weeks he could talk fairly well and recognized and named all objects by touch. He died some months later without any return of palsy or aphasia.

CASE VI.—*Marked dementia, mind blindness, slight amnesic aphasia, and partial tactile amnesia.*

J. M. was an educated man, fifty-seven years old, and had been actively engaged for years in literary pursuits. He had been a heavy drinker, but so far as known had never had syphilis. Early in 1898 he began to be irritable and easily angered and careless about his business affairs, but nothing was suspected of any serious illness until July, when he was suddenly taken ill, becoming delirious and vomiting frequently. He continued to be very excited for several days and then became quiet, but his speech was "a mere gibberish." He was not paralyzed and his speech slowly returned to normal. A similar attack recurred in September. He was alleged to have been blind after both attacks for a short time, but it probably was mind blindness, for he avoided obstacles in walking. He never worked after the first attack, lost all ambition, and was easily controlled.

His general nutrition was good. Gait and station were normal. There was no paralysis of the extremities or cranial nerves. Both knee-jerks were spastic. His voluntary speech was somewhat affected. For the most part he spoke well, but occasionally he would fail entirely to recall a word, or would misuse a word or be compelled to make a paraphrase. He recognized his errors immediately. He understood all that was said to him, but after conversing for some minutes would become a little confused and then his speech would become much worse. He could repeat any word said to him. He could write a few words or short sentences from dictation equally well with the eyes open or shut, but could not read what he had written. Writing soon fatigued him and then he failed entirely. He could not read any writing or print. He could not recognize any object by sight, but knew there was something before him and whether it was longer than broad, or whether it was larger or smaller than some other object shown him at the same time. He recognized the nature and uses of a few objects on handling them, and described them by paraphrase, but could not recall the names. The great majority of objects he did not recognize by touch at all. There was no disturbance of sensibility in either hand. Dementia at first slight, later became quite marked. He had then no realization of the fact that he was a seriously ill man. On the contrary he was overhappy, but had no definite delusions of grandeur. He had lost all intellectual interests. There was a double murmur at the aortic cartilage, hypertrophy of the heart, and the radial and temporal

arteries were much thickened. He had no subjective symptoms of heart disease. The most accurate diagnosis of his case is organic dementia caused by diffuse cerebral degeneration. Though the mind blindness, aphasia, and tactile amnesia increased his dementia, they were not its primary cause, because it began before they appeared.

CASE VII.—*Word blindness and partial tactile amnesia coming on after a sudden hemiplegia and followed by complete dementia, caused by arterial sclerosis and brain tumor.*

The patient was a merchant, fifty-five years old, who about nine months before I first saw him suddenly became hemiplegic. He was a fairly well-built, elderly man. His gait was slightly paralytic and at the same time spastic. There was not marked hemiplegia, but slight athetoid movements were constant in the right arm and were made worse by any voluntary muscular effort. Both knee-jerks were increased, the right being the greater. The right grip was weak, the left good. Babinski jerk was present in the right foot. Speech was normal and he understood everything said to him. He could not understand writing or print except single letters and a few short words. He recognized and named all but a very few objects at sight. He could recall the names of only a very few, though he recognized them. He could recognize and name a few objects by touch; others he recognized, but could not name; but by far the greater number he neither recognized nor named. He could not write with the right hand and any attempt to do so greatly increased the athetoid movements. With the left hand he could write many letters and a few short words. In the left hand sensibility was normal, but in the right two points of contact had to be widely separated to be distinguished. The right pupil did not react to light, the left reacted feebly; both reacted well with convergence and accommodation. There was quite marked optic atrophy on both sides.

A few months later he had a general epileptiform convulsion, and several weeks later awoke one morning speechless except for the words "yes," "no," and "doctor." In the course of a few days speech returned. Several months later he had six general convulsions in one day. Once he had an attack of transitory blindness and jargon speech. As time passed he grew weaker on the right side and his mental state deteriorated. His memory became very poor. He failed to recognize relations and friends, sank into complete dementia, and died.

At necropsy a large tumor was found infiltrating the whole left parietal lobe and the anterior part of the occipital lobe. It did not pass the fissure of Rolando anteriorly. Microscopically it proved to be a sarcoma. The cerebral arteries were all very atheromatous, and many small areas of softening were present in both hemispheres. There was mitral and aortic valvular disease, hypertrophy of the heart, and chronic interstitial nephritis. The lesions were so widespread that the case could not be used to locate any function.

DIFFICULTIES IN THE DIAGNOSIS OF BRAIN ABSCESS.

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LARYNGOLOGIST AND OTOLOGIST TO THE GERMAN HOSPITAL, PHILADELPHIA.

Spiller, in a very able article, says that the "diagnosis of brain abscess depends chiefly upon the signs of some more or less rapidly developing lesion of the brain, with the discovery of a purulent process in the body, or a wound of the head. Abscess of the brain without any evidence of pus elsewhere may be extremely difficult to diagnose." Aurists are rarely concerned with cases other than those having a history of suppuration with the principal focus in the ear. It is not the purpose of this paper to take up the diagnosis of brain abscess, but rather to point out some of the difficulties. Almost every operation is undertaken with some doubt in the mind of the operator. Nothing is clear until the abscess cavity is opened or an autopsy shows the lesion.

The cardinal symptoms of cerebral abscess are neuroretinitis or choked disk, subnormal temperature, headache, chill, vomiting, slow pulse, slow cerebration, stupor, high leukocytosis with high polymorphonuclear percentage, and cerebrospinal fluid free from pus. Cerebellar abscess frequently gives no characteristic symptoms. The diagnosis is best given in Dana's cerebellar seizure, viz., sudden unexpected attacks of extreme vertigo, roaring in the head, relaxation of the limbs, and falling to the ground in a semiconscious state. Sachs calls attention to a symptom that may help at times, that is, the early involvement of the facial nerve, not paralysis, but reactions of degeneration. He claims that the early development of reactions of degeneration in the facial nerve indicates the probability of an abscess in one of the lateral lobes of the cerebellum rather than a sphenoidal abscess.

Unfortunately our cases usually do not present groups of symptoms sharply defined. The changes in the fundus of the eye are generally late; their absence, therefore, is not a help. The temperature is frequently subnormal, but sometimes does not fall below 101° F. The slow pulse is a reliable guide when present, but in some cases it never goes below 80, keeping in perfect accord with the temperature. The headache and slow cerebration are nearly always present, with stupor as a later symptom. Kernig's sign may be present, but is more generally absent; it is almost constant in meningitis.

It may be said that localizing symptoms of brain abscess are practically never present if the abscess be small, and they are frequently absent even when the abscess is of considerable size. Abscess of the frontal lobe is usually attended with no localizing symptoms, unless it is situated about the base of the third frontal or ascending frontal convolution. If the abscess is large the pupil of the same side is usually dilated; if small, the pupil may be sluggish and contracted

If a temporosphenoidal abscess be small there are usually no localizing symptoms; when large the adjacent centres and nerves are likely to be affected, either by pressure or inflammatory action. Hemiplegia on the side opposite the lesion is occasionally found in large abscess. Facial palsy may be caused by lesions in the tympanic antrum, or it may be due to a cortical lesion. In the former case the paralysis is complete; in the latter, the patient is usually able to move the eyelid. If due to antral lesion it is on the same side; if due to cortex involvement it is on the side opposite the lesion.

Aphasia has been noted in abscess of the left temporosphenoidal lobe; its presence is a help in diagnosis, its absence has no significance, as was noted in 3 of my cases. If it be sensory aphasia, word deafness, the lesion is probably in the posterior part of the lobe; motor aphasia, in the anterior portion. Paralysis of the third nerve is sometimes seen in large abscess of the temporosphenoidal lobe, and when complete the picture is characteristic: ptosis, external strabismus, and fixed and dilated pupil. The eyeball can be moved only outward and slightly downward. The presence of any of these symptoms is a help in diagnosis and localizing of the abscess; their absence has no clinical significance.

It is seen, therefore, that no symptom is pathognomonic; that diagnosis is nearly always difficult, and must be made by the general clinical picture. The patient almost always has an unhealthy, septic look, but this, too, may be absent. The bacteriological findings are helpful only indirectly, as up to the present time no definite conclusion can be drawn.

When meningitis and brain abscess are found together the diagnosis may be difficult or impossible. Such a case came under my care. The possibility of abscess was suspected; at the time of operation the bone over the dura was found to be destroyed for an area about 2 x 3 cm., but the dura was covered by healthy granulations. These were cleared away and the membrane was found to be considerably congested, but there was no opening, no marked pressure, and there was a good pulsation. Following operation the patient showed a typical clinical picture of meningitis. The temperature ranged from 102° to 103° F.; the pulse from 100 to 110 and was steady. Kernig's sign was present. Lumbar puncture gave apparent relief and showed some pus with streptococci. There was no change in either eye, and no stupor; but the patient was irritable and rather excitable. There was no vomiting; no chill; no aphasia. The patient died seven days after the operation, and the autopsy showed a small abscess in the left temporosphenoidal lobe.

In another case a laborer had had a history of suppuration of the middle ear dating back twenty years. For about a week before admission to the hospital he had complained of intense headache.

On the day of admission he suddenly became unconscious just after eating his breakfast. He was brought in threshing his arms

about like flails and had to be strapped. He talked in a rambling manner. Once, after admission, his pulse was 62. There were no changes in the eyes; he vomited once. In the absence of all other indications the brain was explored. There was very great pressure and full pulsation; but after a careful search I failed to locate the abscess, and as the patient apparently was sinking rapidly he was sent back to bed. He died ten hours after the operation, and the autopsy showed a small abscess below the first temporal convolution on the left side.

Another patient was seen two hours after admission to the hospital. Her mental state was such that a reliable history could not be taken. She was constantly crying out, "Oh, my head! Oh, my head!" When spoken to sharply she would rouse and answer questions sometimes apparently consciously, at other times in a rambling fashion. She referred her pain to the left side.

Apparently she had had a discharge from both ears for some years. Once after admission, with a temperature of 101.6° F., her pulse dropped to 64. There was no chill and no vomiting. The eye-grounds showed both disks well defined, but the left not quite so sharply. The disk and retina were transparent; there was no change in the vessels. They had the appearance, in the opinion of Dr. Wm. T. Shoemaker, of the probable initial stage of meningitis.

A radical operation was performed at once, but no communication with the cerebral cavity was found. It was thought best to study the patient before going farther, since all of us have seen cases with symptoms of abscess fully as pronounced, or even more so, clear up under the radical operation. Just a short time previously I had operated on such a patient whose condition cleared up nicely, even with a pulse of 60, marked changes in the eye-grounds, sluggishness and vertigo, vomiting and headache.

The day following the operation the patient was much improved in every respect. She was bright and intelligent and hungry and each day showed apparent improvement. She now gave the following history: Scarlet fever at five years, with diminished hearing following. Diphtheria at twelve years, with discharge at irregular intervals from both ears. Had had a paracentesis performed seven years ago. One week before admission she had a throbbing frontal headache; vomited a few times and was very restless. Says there was considerable swelling over the mastoid, but there was none when admitted. The differential blood count was rather startling. Leukocytosis of 15,000 with polymorphonuclear percentage of 89. Cultures showed a short chain streptococcus. This with her variable pulse was sufficient to call for careful watching. But she felt so well and looked so well that my confidence in the polynuclear percentage was wavering.

On the seventh day she complained of headache again; was not feeling so well; when I saw her in the early afternoon she looked septic; her pulse had touched 52, and she was distinctly worse. She

was at once taken to the operating-room and an abscess of the temporosphenoidal lobe, holding 75 c.c. of pus was evacuated. Her recovery from this time on was uneventful.

This patient was right-handed, but there was no aphasia. In the 3 cases mentioned there was complete failure of a possible localizing sign, aphasia, for in a right-handed person we would usually find the centre of speech on the left side. The second case was a boy admitted to the Children's Hospital in the service of Dr. Randall. It was owing to his absence from town that the patient came under my care, and it is due to his kindness that I am permitted to report it.

The patient was admitted on the afternoon of July 9, and operated on the following day. The radical operation was done on the right side. Sinus involvement was suspected and a careful search was made, but the parts appeared to be in good condition. The boy did very well until the afternoon of the 14th, when, without chill or other sign, the temperature dropped to 98°, and then rose rapidly to 105°. Owing to the fact of the sinus having been manipulated the possibility of a simple phlebitis was considered and it was decided to wait. But during the evening and early morning hours there was a chill and the temperature dropped to 97° and rose to 106.8° F. He was operated on at noon, and a thrombus was found in the jugular bulb with pus in the sinus. During the first four or five days following operation he appeared to improve. Then he began to have a rather septic look. As the jugular had been tied below the entrance of the facial vein it was felt that there could be no danger from that source. There was no purulent process on the left side. Very slowly, but surely, he was losing ground. A few times he complained of headache. On the seventh day there was some stiffness of the neck; the eye-grounds showed no changes. Kernig's sign was absent. There were leukocytosis of 13,000; polynuclear percentage of 83; and streptococci.

Knowing that a frequent source of infection of the cerebellum is through the sinus it was decided to explore, even though there were no definite symptoms. The route chosen was through the sinus. A small cerebellar abscess was found and drained. Again for a few days there was apparent improvement, but then he began to lose ground and on August 18, not quite six weeks after admission, he died. The autopsy showed that the jugular, the sinus, and the cerebellum had healed completely, but that there were multiple abscesses of both lungs, the liver, and the spleen.

It seems to me that the diagnosis of these conditions is the most difficult part of our work. No group of symptoms will be found infallible and no symptom is pathognomonic. Any one of the symptoms may be present or absent, with possibly one exception. I have come to place great reliance upon the presence of leukocytosis with high polymorphonuclear percentage. If this is 80 or over it has always, in my experience, shown sepsis; not necessarily of the brain.

It may be septic thrombosis or other general septic process, but in my experience its presence has never yet failed to indicate sepsis. Its absence does not contra-indicate sepsis, as shown in cases that have been reported in which even with a high degree of pyemia the polynuclear percentage may be as low as 70. But given a group of symptoms pointing to an infection, the presence of a high polynuclear percentage will, in most cases, be the deciding factor.

REVIEWS.

MODERN MEDICINE. ITS THEORY AND PRACTICE. IN ORIGINAL CONTRIBUTIONS BY AMERICAN AND FOREIGN AUTHORS. Edited by WILLIAM OSLER, M.D., Regius Professor of Medicine in Oxford University, England. Assisted by Thomas McCrae, M.D., Associate Professor of Medicine and Clinical Therapeutics in Johns Hopkins University, Baltimore. In seven octavo volumes; illustrated. Vol. I, pp. 937. Philadelphia and New York: Lea Brothers & Co., 1907.

THE publication of Osler's *Modern Medicine* must be considered an event in the history of medicine in this country; it has been awaited with keen anticipation, and the conviction has been general that it is destined, even more than systems of medicine heretofore published, to influence profoundly medical thought and practice in the English-speaking world and beyond. The purpose in mind and the object of the work are well stated by Dr. Osler in his introduction, when he says: "It is designed primarily for the practitioner who wishes to keep himself informed of the existing state of our knowledge in clinical medicine. Elaborate discussions upon doubtful problems have been avoided, and, as far as possible, a clear statement is given without unnecessary references to the literature. Authors have been selected who are acknowledged authorities, and while it is not always easy for a writer who is saturated, so to speak, with his subject to keep within limits, and to remember the practical character of the men for whom he is writing, I hope we have been able to keep an even balance between the condensation of the text-book and the elaborate treatment of the monograph. The first consideration in a work of this kind is that it should be helpful."

In addition to the introduction by Dr. Osler, the volume contains the following articles: Inheritance and disease, by J. George Adami; diseases caused by physical agents (light, x-rays, electricity, air, heat, and cold), by Alfred Gordon; diseases caused by chemical agents (metallic and other poisons), by David L. Edsall; drug habits (alcohol, opium, morphine, cocaine, etc.), by Alexander Lambert; food poisons, by Frederick Novy; snake poisoning, by Hideyo Noguchi; auto-intoxications, by Alonzo Englebert Taylor; actinomycosis, nocardiosis, mycetoma, oidiomycosis, blastomycosis, pulmonary aspergillosis, and mycosis mucornia, by James H. Wright;

the protozoa, by Gary N. Calkins; mosquitoes, by L. O. Howard; malarial fevers, by Charles F. Craig; black-water fever, by J. W. W. Stephens; trypanosomiasis, by David Bruce; amœbic dysentery, by Richard P. Strong; diseases caused by animal parasites, by Charles W. Stiles; metabolism, normal and in disease, by Russell H. Chittenden and Lafayette B. Mendel; diabetes mellitus, diabetes insipidus, and gout, by Thomas B. Futcher; obesity, by James M. Anders; rickets, by George Frederic Still; and scurvy, by Robert Hutchison.

The range of subjects discussed is so wide and diversified that it is impossible within the limits of a reasonable review to do more than mention the titles of many of the contributions: one must content himself with generalities, rather than undertake a critical review. Most of the contributors have a national, some an international reputation, and their names alone constitute assurance of excellence of accomplished work; indeed, so well known is the association of the author with his work that were those competent to judge asked to designate authorities preëminently fitted to contribute certain chapters, they doubtless would mention Adami, Calkins, Howard, Craig, Stephens, Bruce, Strong, Stiles, Chittenden, and others of the afore-mentioned list.

If the reviewer ventures to select for special comment several of the many articles in the volume, he does so conscious of the excellence of those referred to only casually. Thus, it seems a happy thought that suggested the incorporation of articles on the protozoa and the mosquitoes—articles, at first sight, foreign in scope and nature to a work on medicine. However, although we have scarcely more than begun to comprehend the pathogenetic significance of the many protozoa, we do know that a knowledge of the varieties, structure, and life-history of the mosquitoes is essential in the study and prevention of malaria, yellow fever, and other diseases; so that upon reflection it seems exceedingly appropriate that these chapters, written by acknowledged authorities, should be included; furthermore, they give to the practitioner information nowhere so readily obtainable and nowhere presented in a form so well adapted to his needs.

Several of the articles must be looked upon as really noteworthy contributions to medical literature. Of these, one may perhaps mention first those by Adami, Taylor, and Chittenden and Mendel. During the last twenty years our ideas of heredity in relation to disease have undergone considerable modification in consequence of the studies of Weismann, Mendel, and others, and it is meet, therefore, that we should have such a clear and comprehensive, though withal succinct and authoritative, statement of present opinions on the subject, as Adami gives us. He well separates conditions mistakenly regarded as inherited from those truly inherited. Especially illuminating is his discussion of individual inheritance and the

theories of inheritance, and his exposition of his own conception of a physicochemical theory of inheritance. Taylor's article on auto-intoxication is unquestionably one of the sanest discussions of a subject which so readily lends itself to speculation that we have read during recent years. Particularly commendable is his treatment of gastro-intestinal auto-intoxication, of which he adopts an exceedingly sensible classification—satisfactory alike to the scientist and the practitioner. One minor regret is that the clinical phenomena of the condition have not been more elaborated; but the article as it stands is commended to the attention of all who desire to separate fact from fancy in the realm of auto-intoxication. The discussion of metabolism, normal and in disease, by Chittenden and Mendel, will appear to the scientific physician as the final pronouncement of well-qualified investigators; by the practitioner it will be read with interest if for no other reason than that it runs counter to some of his preconceived ideas in reference to food values. It contains also the results of considerable investigation that may be used by the physician in formulating rules for the dietetic management of disease. This matter of diet is of very great importance, and no investigations have aroused greater interest than those recently conducted by Yale University. If they seem to prove that most persons eat too much, especially too much meat, there is, on the other hand, a large number of competent observers who do not accept the result of these investigations *in toto*, who believe that although certain things may be possible to the human economy, these may not be wise, and that withdrawal of much proteid may occasion undesirable demands upon the reserve power of the system, especially as regards non-proteid metabolism. A sane view of the matter, however, is thus well expressed by Chittenden and Mendel: "One is inclined to emphasize the desirability of using common sense in the application of dietetic rules, remembering that man is well adapted by nature to subsist on a variety of foods. On matters of diet every man should be a law unto himself, using judgment and knowledge to the best of his ability, reinforced by his own personal experiences. Vegetarianism may have its virtues, as too great indulgence in flesh foods may have its serious side; but there would seem to be no sound physiological reason for the complete exclusion of any one class of foodstuffs, under ordinary conditions of life."

In addition to the foregoing, the volume contains a number of articles of much practical and other value. The chapters on diseases due to chemical agents (metallic and other poisons), by Edsall, is of a very high order of merit; and it gives evidence of a first-hand acquaintance with the disorders in question: notably in connection with chronic mercurial poisoning, but also elsewhere. The articles on diabetes mellitus, diabetes insipidus, and gout, by Futcher, are such as a knowledge of his earlier work would lead one to expect: complete, authoritative, practical. Lack of space only

forbids a more detailed mention of the other really excellent articles.

As a whole the volume is a noteworthy addition to medical literature—well conceived, excellently planned, splendidly executed. It reflects, doubtless as he wished, the thoughts the editor had in mind when he wrote: "It cannot be too often or too forcibly brought home to us that the hope of the profession is with the men who do its daily work in general practice. Our labors are in vain—all the manifold contributions of science, the incessant researches into the complex problems of life, normal and perverted, the profound and far-reaching conclusions of the thinkers and originators—all these are *Nehushtan*, sounding brass and tinkling cymbals, unless they result in making men better able to fight the battle against disease, better equipped for their ministry of healing. Gradually, often insensibly, the practical advances of the laboratory and of the hospital reach the men with whom, after all, rests the final testing of our efforts. The work in practical sanitation, the last word in the prevention of disease, the carrying out new methods of treatment, the exchange of the old accoutrements for the new weapons and the new methods of warfare, these rest with the rank and file of the profession who make effective and translate into practice the new knowledge."

Volume I being a foretaste of what is to come, Osler's *Modern Medicine* may be warmly recommended to the physician as replete with the practical applications of science to medicine, mirroring the clinical manifestations of disease, and helpful and resourceful in suggestions for treatment. A. K.

A Study of Human Bloodvessels in Health and Disease. By Arthur V. Meigs, M.D., Physician to the Pennsylvania Hospital, Philadelphia. Pp. 136, with 103 original illustrations. Philadelphia and London: J. B. Lippincott Co., 1907.

The reader who takes up this volume with the expectation of finding it a systematic treatise upon vascular disease will be disappointed. It is a book of personal observations and interpretations, and nowise a compendious or systematic presentation of the pathological changes to which bloodvessels are liable and which they frequently exhibit. The book is based upon a series of excellently executed illustrations made by the eminent medical artists, the Fabers, from microscopic preparations studied by Dr. Meigs; and in fact should be considered as an atlas, with the text mainly made up of explanatory descriptions of the drawings and entering but little into further analysis and discussion than such description entails or into attempt at correlation of the author's findings with the work of other students. The bulk of the preparations have been made with borax carmine as the stain; and from the outstart the author, therefore, largely

limits his scope to features which this reagent yields, and misses much really valuable information which some of the more differentiating special methods of staining would have revealed. The text includes chapters upon the structure of arteries, veins and capillaries, new bloodvessels, diseases of bloodvessels in general, diseases of the radial arteries and veins, bloodvessels in inflammation, tuberculosis and syphilis, the bloodvessels of the heart, lungs, liver, spleen, kidney, and of the brain and spinal cord. That the mode of presentation has opened the way for unnecessary and undesirable repetition of statement, into which unfortunately the author has fallen, is an entirely fair criticism; and that for the comprehensiveness of the title and the ambitious appearance of the volume the treatment is too discursive and the isolated subjects in too unfinished a state seems to the reviewer an equally just comment. The author's views would have gained added force had he grouped his material and illustrations upon this or that type of vascular disease instead of distributing, without actual addition, his statements and examples over the general and various special chapters; at any rate such method would have ensured a greater economy of pages and would have saved the author the self-confessed imperfections of most of his special chapters.

These strictures are presented in good faith and with no intentional carping criticism. It is realized full well that the volume was not published as a text-book or treatise but rather as a record of observations made as a life heavy with the duties of the active practice of medicine have permitted; yet if in future editions the method of arrangement could be altered by condensation and subject rearrangement, and if a closer correlation and fuller study of some of the more interesting and important features could be attempted, the book would surely gain much in excellence.

As it stands there is contained in the volume much food for thought; and the acuteness of the author's power of observation and the originality of his interpretations make it a very suggestive book and one well worth perusal. In the first chapter the demonstration that the artefacts due to shrinkage of vessels in fixation and preservation may be responsible for mistaken recognition of various irregularities in the walls of both arteries and veins, but more markedly in the latter, is very successful; and differences of appearance given in the coats of vessels into which suitable glass rods or tubes have been inserted before fixation in comparison with those afforded by vessels ordinarily prepared, are striking and worthy of remembrance. Minor thickenings of the intima are clearly shown to be possibly nothing more than such artefacts and not necessarily to be regarded as evidence of disease. The observations upon the structure of the vena cava and the cardiac sinus venosus deserve close attention (absence of circular muscle layer from the wall of the vena cava; lack of differentiation into the usual coats, and absence of smooth muscle from the wall of the sinus venosus, which consists merely of a thin fibrous

intima merging by a loose fibrous tissue directly with the tissue of the myocardium). In the chapter upon capillaries the author proposes a theory of the evanescent character of these tubes which the reviewer feels is very unlikely to meet with any ready approval or acceptance. He compares the capillaries with the little rills of water which form between blades of grass after a heavy rain, trickling forward to join in greater and greater volume until poured into some permanent stream, but disappearing as the ground surface dries. "They may be truly said to be ephemeral, for they open in the tissues as the need for them arises and close and disappear when their usefulness has ceased. . . . It is certain that capillaries are ephemeral and often return to their primitive state by giving back their walls again to form simple connective tissue. . . . The capillaries, on the other hand, are nothing but tubes hollowed out in the connective tissue with which they are surrounded. If a single capillary running in any tissue by itself is empty it becomes at once and without any change a string or fiber of connective tissue." (Pages 17 and 19.) Undoubtedly with varying grades of fulness the capillaries vary in ease of recognition, but the reviewer is entirely unwilling to subscribe to the author's statement of the complete conversion of their endothelial structure into strings or fibers of connective tissue and the reassumption of the plate-like character of their cells with alternate grades of emptiness and fulness of the tubes. Examination of the largely bloodless and shrunken tissues of a microscopic preparation of autopsy material is far apart from examination of living structures; and observation of such preparations as a frog's mesentery, foot-web, or tongue in the living animal before inflammatory changes have set in, give an impression of capillary fulness and ubiquity in the tissues very much at variance with the author's fancy. That under pathological conditions with due time capillaries may form anew and are often also in time destroyed and contribute to connective tissue goes without saying at the present day; but were it a serious question the proof of the incorrectness of Dr. Meigs' surmise would not be difficult of demonstration. His own criticism of the old idea of the incompleteness of the capillary arrangement in the spleen, necessitating a diffusion of blood in splenic pulp (p. 114), if applied to other structures of the body can with difficulty be harmonized with such ideas. In his chapter on new bloodvessels there is much of interest in the suggested formation of capillaries in the manner of vessel development in the embryonic vascular area. This mode of vascular production in pathological processes has never been successfully made out; but the observation of capillary growth within a tissue, which to the reviewer's mind is hyperplastic endothelium, is at least suggestive, not so much in the mere formation of the vessels, since it is quite possible that they may have been the usual capillary penetrations from the nearby vasa vasorum, but in the features which the author interprets as evidence of their formation independently

of any other vessels. Should Dr. Meigs' views come to prevail in this matter alone, after due study and confirmation, his whole volume would be well justified. In this same chapter the magnificent etching of giant cells (Fig. 25) is an admirable argument for the belief in the vascular origin of these structures in tubercles; and the author's view that they represent abortive attempts at vascular formation, while not established by his demonstration, is surely worth serious consideration and study. Probably the best chapters in the volume are those upon disease of bloodvessels in general and upon disease of veins; and of the particular features of these parts the best is the clear demonstration of the frequent and important involvement of veins by sclerotic disease, and the more ready invasion of venous than arterial walls by acute inflammatory infiltrations. Here, as well as elsewhere in the volume, the demonstration of well-marked sclerotic changes in the vessels of the young, notably in several children, is a feature of decided value. Of the special chapters, as might be supposed from the author's previous writings, that upon the bloodvessels of the heart, repeating his well-known demonstration of the intramuscular as well as intermuscular situation of the myocardial capillaries, and demonstrating them by injection preparations in addition to his previous studies on non-injected preparations, is the most satisfactory.

All through the volume occur expressions and views with which one could if so disposed take quick exception, for example, the author's very evident lack of sympathy and neglect of modern views of the importance of microbic influence in the origin of disease (p. 99) or his refusal to recognize anything morphologically peculiar in the nodular groupings of cells in tubercle formation (p. 69); but the reviewer prefers to avoid the really needless discussions which would be entailed by their consideration. The pictures upon which the book is based are very valuable, and are presented with an enviable luxury, being printed upon inserted sheets of a well-calendered paper and accompanied with full legends upon the opposed tissue cover. The reviewer has noted only one typographical error (p. 81, line 10, substitute "recognized" for "reorganized"); and the whole mechanical work is good. A. J. S.

A Text-book on Prescription Writing and Pharmacy. By Bernard Fantus, M.D., Professor of Materia Medica and Therapeutics, College of Physicians and Surgeons, University of Illinois, Chicago. Second edition, pp. 404. Chicago: Chicago Medical Book Co., 1906.

If one may select that in which this book appeals to him above the rest, he would state that in making every endeavor that the student shall become proficient in prescription writing, the author

has achieved remarkable success: not only that prescriptions shall be in unimpeachable terminology, but that the student shall originate prescriptions adopted to the requirements in the special instance of disease and the particular patient suffering from it. Not only in calling attention to the externals, those small matters which indicate the man of science, but in citing especial instances of bad form, the author presents the questions of determination of quantities, the composition of prescriptions, covering also modes of administration of remedies, and closes his first part with sensible suggestions in prescription ethics. Part II, Pharmacy, covers the various classes of preparations, with frequent examples of what the student will designate as "good prescriptions." Part III is a reference list of official drugs and their preparations, and contains much information in small space which the student will find useful in formulating his therapeutic endeavors; for instance, the name with indicated pronunciation, the genitive, the definition, description, solubility, incompatibles, uses in brief, and method of administration. The student who acquires this will learn not only how to prescribe elegantly, but as well will acquire considerable pharmacological and therapeutic information. In the appendix is found a few suggestions for laboratory exercises. These we regard as essential and if carefully taught with blackboard exercises in writing, the future physician will appear in a higher scientific position than the pharmacist has given him credit for. We would especially commend this work to those compilers of inspired therapeutic literature based on selected formulæ of eminent physicians so frequently met with in trade circles. We feel that a study of this book will conduce not only to more elegant, but as well to more effective therapeutics.

R. W. W.

PARAFFIN IN SURGERY: A CRITICAL AND CLINICAL STUDY. By WILLIAM H. LUCKETT, B.S., M.D., Attending Surgeon, Harlem Hospital, and Surgeon to Mount Sinai Hospital Dispensary; and FRANK I. HORN, M.D., Assistant Surgeon, Mount Sinai Hospital Dispensary, New York City. New York: Surgery Publishing Co., 1907.

THIS little monograph presents in a concise form a good deal of original work as regards the use of paraffin in surgery. Its authors present successively the subjects of the chemistry of paraffin, its early and late disposition in the tissues, the technique and armamentarium required for its injection, and the unsatisfactory results and accidents which occur from its use. As to its disposition in the tissues, they hold, as a result of microscopic sections made immediately after its experimental injection into the tissues, that the

early disposition of paraffin is a mechanical and physical distribution in the tissues. They believe that they have furnished conclusive proof of the disinclination of pioneer cells, fibers, and blood-vessels to permeate the mass of paraffin. Their experiments also show that paraffin in the tissues becomes encapsulated, consisting of new tissues formed from tissues encircled by paraffin at the time of the injection; accordingly encapsulation takes place from the inside as well as from the outside. They consider that the accidents which have occurred, such as amaurosis and pulmonary embolus, are attributable to the use of paraffin with too low a melting point. They recommend the use of paraffin at a melting point above 110° F. The last section of the book is occupied with reports of cases in which they have used paraffin injections. Whereas of late the pendulum is swinging violently in the direction of too great depreciation of the value of paraffin in surgery, the authors' efforts to throw some real light on the subject are most commendable, and their conclusions show that, if properly utilized, paraffin is a most valuable therapeutic agent. F. R. P.

THE EAR AND ITS DISEASES. A TEXT-BOOK FOR STUDENTS AND PHYSICIANS. By SETH SCOTT BISHOP, B.S., M.D., LL.D., Honorary President of the Faculty and Professor in the Post-graduate School and Hospital of Chicago. 27 colored lithographs and 200 additional illustrations; pp. 440. Philadelphia: F. A. Davis Co., 1907.

THIS work is an amplification of the section on the ear which was included in the author's previously published book on *Diseases of the Nose, Throat, and Ear*. Dr. Bishop deserves to be heartily congratulated upon the result of his labors. In the present volume he has covered the entire subject of otology in the most comprehensive manner, and as his literary style is concise and lucid, within the upward of four hundred pages which were at his disposal, the reader may search in vain for sins of omission.

The opening chapters on the anatomy of the ear are very fully illustrated, chiefly with original drawings from the author's specimens. In fact, the illustrations are a noteworthy feature throughout the entire work; the only criticism to be made in regard to them is that there are several which might be deemed superfluous, such as the interior of an office and of an operating room. Dr. Bishop has devised an excellent case record, one of the most practical we have ever seen. All of the topics written of are thoroughly well handled. This is particularly true of the section dealing with chronic adhesive middle-ear inflammation. The author advances more

ingenious and practical methods of treatment for this *bête noir* of the aurist than are usually described, and shows an amount of common sense and judgment that is too often wanting when various plans of treatment are under consideration. He is properly emphatic in warning against injudicious overtreatment of the sclerosed ear.

We do not know when we have reviewed a book written on otology and meant for the use of students and general practitioners, as well as specialists, in which so much of real value to all of the three groups mentioned is combined. Dr. Bishop's book is admirably adapted for use as a text-book and as a book of reference.

F. R. P.

METABOLISM IN PRACTICAL MEDICINE. By CARL VON NOORDEN. Vol. I, The Physiology of Metabolism. By ADOLF MAGNUS-LEVY. Anglo-American issue, under the editorship of I. WALKER HALL. Chicago: W. T. Keener & Co., 1907.

ONE very commonly hears expressed a desire for an authoritative, philosophical discussion, in a manner that can be appreciated by the intelligent general practitioner, of the results of the vast amount of work that has been done in comparatively recent years on metabolism. The studies of this subject have been so very numerous, and have, in large part, been carried out by such relatively technical methods, that many intelligent practitioners have only a hazy idea of the actual value of the results; and, in ordinary circumstances, it is practically impossible for them to clear up their conceptions without undertaking a very laborious study of the literature of the subject. The work of which this is the first of three volumes in large part fills this want. Von Noorden's original *Pathologie des Stoffwechsels* was of great value to the special student of metabolism, but not very interesting to the clinician who had no such special interest: because it was largely a concise statement of figures and conclusions. In this present new and greatly elaborated edition of this work he has associated with himself a group of the most important of the workers on metabolism in Germany, who have taken up subjects concerning which they speak with authority; and the questions are discussed from a much broader and more philosophical standpoint, and in a manner that it is both interesting and comprehensible to the practitioners in general.

The only unfortunate thing about the work is its size, which will, both from the standpoint of cost and from that of the labor involved in going through it, interfere to a considerable extent with its being widely read. Those, however, who have the moderate amount of energy demanded to read it will find it a most valuable and inter-

esting discussion of all the important questions concerned in metabolism, so far as our knowledge at present goes. The only point to which serious exception can be taken is, perhaps, that the authors limit themselves rather too much to a consideration of German literature, largely to the exclusion of work done outside of Germany; but, this being a common custom with German authors, it deserves no special emphasis here.

The reviewer's acquaintance with the German edition of this work leads him to feel that the present volume is the most valuable to practitioners of medicine, because it especially well gives them increased breadth of view; the other volumes dealing with more detailed subjects. The author of this volume, Magnus-Levy, as would be expected from his various writings, takes a broad, firm, and interesting point of view in his manner of discussing the subject; and gives fair credit to all sides of any contentions. He takes up the foodstuffs, digestion and absorption, the fate of the foodstuffs in the tissues, total energy exchange, nitrogenous metabolism, the influence of muscular work, and various other such factors. It is an exceedingly valuable work and the English-speaking profession should be grateful to have a translation of it. D. L. E.

ALCOHOL. THE SANCTION FOR ITS USE. Translated from the German of J. STARKE. New York and London: G. P. Putnam & Sons, 1907.

POPULAR and semipopular books on important scientific subjects are, as a rule, of questionable utility; and they are likely to be very harmful, if they are so prepared that they readily lead persons astray. The common statements regarding alcohol in the text-books on physiology used in the public schools are, as a rule, both ludicrous and harmful. These statements are usually violently against alcohol. The book at present under review takes the contrary standpoint, and gives a most absurd discussion of the value of alcohol to humankind; and it is likely to do a good deal of damage, because it is written for the laity.

From the scientific standpoint, a review of the book is superfluous. There are many details that are extremely entertaining, because they are so funny; but the fairest method is perhaps to close the review by quoting a sentence that the author introduces after a somewhat involved discussion of the difference between a "weak character" and a "weak mind." "In short, and the reader will agree with me, it is not prudent to go into too much detail in this matter."

D. L. E.

PROGRESS
OF
MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Mouth Disinfection in the Prophylaxis and Treatment of Pneumonia.—WADSWORTH (*Jour. Infect. Diseases*, 1906, iii, 774) has studied the effect of disinfection of the mouth in the prophylaxis and treatment of pneumonia, his studies comprising cultural, morphological, and animal experimentation, and the effects of simple isotonic salt solutions, alcohol, different bland solutions, and various commercial solutions. Among his conclusions the following points may be noted: His own observations confirm the results of previous studies that complete disinfection of the mouth is impossible, but from tests and experiments the practical value of many of the antiseptic procedures commonly employed in mouth disinfection was accurately determined. Pneumococci, as compared with other pathogenic bacteria, are extremely susceptible to the plasmolytic action of saliva and alkaline solutions and also to the antiseptics which act in this way. The susceptibility to antiseptics in general varies greatly and especially under different conditions. In broth media pneumococci are readily destroyed; in exudates, albuminous material and detritus interfere with the action of many antiseptics. Sputum disinfection by harmless solutions is extremely difficult. Of all the commercial solutions studied—listerine, borine, borolyptol, glycothymoline, odol, and Seiler's solution—none proved efficient when tested on pneumococci under conditions most favorable for their action. Formalin, lysol, and hydrogen peroxide failed to act on the pneumococcus in exudates; in short, alcohol alone of all the antiseptics studied proved efficient when tested on pneumococci under all the conditions of the experiments. Observations on the diffusion of different solutions in the secretions of the mouth under different conditions showed that the presence of salts in isotonic quantities and alkalies was of positive, if

slight, value. Rapid diffusion obtained with alcoholic solution was greatly accelerated by the addition of glycerin. Hot solutions are better. In the practical studies on pneumonia patients, simple isotonic solutions are only slightly efficient; but with an alcoholic wash many of the bacteria are destroyed, the contaminated secretions are more rapidly removed, and at the same time disinfected, and finally the natural resources of the tissues are more safely and efficiently aided in the elimination of the infectious material. Thus, alcoholic solutions containing glycerin and salts in bland quantities were in every particular more efficient than any of the washes hitherto recommended for mouth cleansing or disinfection and alone possess practical value. 30 per cent. of alcohol is the strongest solution that can be used habitually, and the weakest to give for reliable disinfection. This disinfection should be urged most emphatically on each individual, owing to the ease of spreading the infection by the transfer of the infectious material by coughing or sneezing, especially when in crowded communities. The formula Wadsworth found most suitable was as follows:

℞—Sodium chloride. (C.P.)	2.0	½	dram.
Sodium bicarbonate. (C.P.)	0.7	10	grains.
Distilled water	60.0	2	ounces.
Glycerin	30.0	1	ounce.
Alcohol	150.0	5	ounces.
Thymol, Menthol } of each	0.07	1	grain.
Oil of wintergreen		3	drops.
Oil of cinnamon		2	drops.
Oil of eucalyptus		5	drops.
Tincture of cudbear	6.0	1½	drams.
Tincture of rhatany	2.0	½	dram.—M.

S.—Dilute with an equal volume of water before using.

The Opsonic Index and the Antipneumococcal Power of the Blood in Pneumonia.—H. E. Wolf (*Jour. Infect. Diseases*, 1906, iii, 731) gives a brief summary of the work of Wright and Douglas, Mennes, Hektoen, and Neufeld and Rimpau and their results obtained in conditions other than pneumonia. He experimented with different dilutions of normal and pneumococcal serum and his method of work is outlined. It was found that dilutions of 0.025 c.c. gave the most satisfactory results; the pneumococco-opsonic indices in the charts are based on results so obtained. 14 cases were studied by this method, usually with daily determinations, before the crisis in typical cases, and less frequently afterward. 2 cases were complicated with empyema, 2 were of a migratory type, and 5 were typical lobar pneumonias ending with crises. Besides the opsonic index, leukocyte counts and blood cultures were made, and are indicated in the interesting charts for comparison. The typical cases had much in common. The opsonic index persisted below normal until within a few hours before the crisis (this corresponds to the negative phase of Wright), then rose and reached a maximum within twenty-four hours after the crisis; then followed a slow decline to normal. During the same time the leukocyte curve rose with the chill and temperature and began to decline as the opsonic index rose; thus although the individual pneumococco-opsonic index of pneumonic blood may be below normal early in the disease, yet due

to the increase in the leukocytes, the antipneumococcal power of the same may be much above the normal, assuming, of course, that the opsonin present is sufficient to opsonize the quota of pneumococci necessary. Rosenow's observations (*Jour. Infect. Diseases*, 1906, iii, 683) on the pneumococcidal action of polymorphonuclear leukocytes *in vitro* support this view. This is shown very graphically in one of the charts. In one of the cases of migratory pneumonia, the pneumococco-opsonic index remained persistently below normal, rising a little with the clearing up in one lobe, but falling the next day when the other lobes were involved. At last on the twelfth day they rose above normal and continued so throughout the period of delayed resolution until complete recovery.

In the fatal cases examined the opsonic index continued to fall until death. The leukocytes, though high, fell steadily during this period. Two interesting experiments were performed on normal, healthy men. In one the injection of dead, virulent pneumococci gave some local inflammatory signs with an increase in temperature and leukocytes, with at first a drop in the opsonic index (negative phase) and then a rapid rise above normal with a coincident drop in the number of leukocytes. In a second experiment with dead avirulent pneumococci, somewhat similar effects were noted in the temperature and leukocytosis, but there was no increase in the opsonic index. This indicated that the property of virulence may be somewhat concerned in the stimulating of the production of immune opsonins.

Wolf then notes the effects of injection of pneumococcal opsonins in 14 cases; 11 recovered, 3 were fatal. In all cases ending favorably there was a slight increase in temperature four to six hours after injection and an increased leukocytosis. Crisis occurred in from eighteen to thirty-six hours after injection in all but one case, in which a second injection was given and crisis followed in eighteen hours. The opsonic index rises characteristically just before the crisis. There was no exaggeration of the negative phase immediately following the injections. In 5 cases the crisis occurred on the third day, 3 on the fourth, 1 on the fifth, and 2 on the sixth. These cases were chosen at random from different patients, with a mortality of about 40 per cent. for that month in the hospital. Hence the recovery among the infected patients seemed to be high and crisis occurred early. Of the 3 fatal cases 2 were senile pneumonias, while the others showed a marked hypoleukocytosis. After injection there was no marked reaction in the temperature or leukocytes and no change in the opsonic index, possibly indicating that the sources of vital resistance of the body had been so exhausted as to permit of no further stimulation. His conclusions are as follows: (1) In pneumonia the pneumococco-opsonic index is first decreased, but it rises in favorable cases, reaching its height soon after the crisis, while in unfavorable cases it remains persistently low. (2) The estimated total antipneumococcal index (estimated from the leukocytic index and opsonic index) is early increased and remains high until crisis is complete in cases with a favorable termination. (3) Pneumococcal exudates contain little or no pneumococco-opsonin, nor do they exert any antiphagocytic action. (4) Dead virulent pneumococci produce a similar evolution in the antipneumococcal index in normal persons to that which occurs in pneumonia. (5) Dead avirulent pneumococci have

no effect on the pneumococco-opsonins. (6) Treating patients with lobar pneumonia with antipneumococcal vaccines seems to exert a favorable influence upon the course of the disease, as indicated by an apparent decrease in mortality and by early crisis, but a great deal of further work is necessary before any conclusions of final value may be drawn.

The Functions of the Muscles and Nerves of the Arteries.—GRUTZNER (*Deutsch. Arch. f. klin. Med.*, 1906, lxxxix, 132). The earlier work of Claude Bernard, Ludwig, and Heidenhain established the existence of dilator and constrictor fibers to the arterial muscles and showed the importance of their action in maintaining and regulating local and general blood pressure. The question arises whether this stop-cock action of the arterial musculature is its only function. Senac was the first to suggest that the arteries through their muscles serve not only to widen and constrict the flow-bed, but take an active part in the propulsion of the blood. "The arteries," he says, "are real hearts of a different form." This view was strengthened by the observation of Schiff that the arteries in the rabbit's ear may be seen to contract in an orderly sequence from base to tip. Many facts have been adduced to sustain the existence of such a propelling force in the arteries. That the arteries are empty after death and the veins filled is one. It has been observed that the circulation continues in the frog's foot for some time after the heart is tied off. Bezold and Goldscheider observed that after tying off the heart in rabbits the pressure in the carotid and in the vena cava were about the same, namely, about 86 mm. of water. If the cervical cord were severed and the vasomotor nerves thus cut off the arterial pressure was 86.6, the venous 43.4. If the vasomotors in the severed cord be stimulated the venous pressure will rise; for example, from 50 mm. to 75 mm., while the arterial pressure falls. Grützner also points out that when sensory nerves are stimulated there is a rise of blood pressure which Ludwig explains by a constriction of the splanchnic area, but the same rise occurs when the whole splanchnic area has been ligated off. Such a procedure should cause a dilatation of the muscle and skin vessels, and unless we assume that the arteries themselves have some propulsive power it is difficult to understand how the pressure is increased. The distribution of the muscle fibers, too, is an indication of their purpose. They are most numerous in the small arteries where the force of the heart becomes spent, and particularly abundant in places where special difficulties must be overcome, as in the intestinal capillaries. The strong musculature of the vena porta and of the umbilical artery indicates a response to the demand where most assistance is needed to carry on the circulation. The capillaries possess no muscles, but they may dilate and contract by means of the surrounding Rouget-Meyer Korpzellen. The veins have muscles and no doubt assist in propelling the blood. Goltz has shown that paralysis of the abdominal veins renders the circulation impossible, the animal bleeding to death into its own veins. The venous sacs with rhythmic contractions in some of the lower animals offer suggestive analogies. From the clinical side similar conceptions of the importance of the vessels in assisting the heart action and in controlling the distribution of the blood have come from Rosenbach and Hasebroek.

Diseases of the Large Bloodvessels in Congenital Lues.—RACH and WIESNER (*Wien. klin. Woch.*, 1907, xx, 521), in an examination of 27 cases of severe and mild congenital lues, found lesions of the aorta or pulmonary artery in 16. The lesions are most frequently situated just beyond the point of origin of the aorta and at the orifices of the large arteries, at which points the vasa vasorum are most numerous. They consist histologically of an infiltration with small and large lymphocytes and a few polymorphonuclear leukocytes and proliferation of the connective-tissue cells of the adventitia and neighboring layers of the media. The changes are most marked immediately about the vasa vasorum and frequently lead to obliteration of their lumen. In some instances there is degeneration of the elastic fibers of the media. In the descending aorta of one case an elevated plaque was found on the intima consisting of fibrillary connective tissue poor in cells. The elastic lamellæ were separated and many of their fibers destroyed. Such changes in the intima and media are rare. The lesions in the bloodvessels bear no relation to luetic disease of the other organs. The one may be severe while the other is slight. Careful search failed to reveal spirochetæ in any of the lesions and the authors are inclined to view them as toxic in origin. The frequency with which the arteries are affected in congenital lues suggests an etiological factor for many cases of arteriosclerosis of unknown origin in children. Such early lesions may too be a predisposing factor in the development of arterial changes in later years.

The Causes of Orthopnœa.—HOFBAUER (*Ztschr. f. klin. Med.*, 1907, lxi, 389) takes exception to the prevalent view that patients with dyspnœa assume an upright posture because this position facilitates the action of the accessory muscles of inspiration and relieves the chest from the pressure of the body weight. Such a simple explanation does not satisfactorily account for the increased difficulty of breathing which so commonly comes on during the night. Some other factor must be at work. In cases of pleural disease Hofbauer has shown by carefully studied tracings that the dyspnœa is expiratory in type, the difficulty being in getting the air out of the lung and not in getting it in. The dyspnœa depends upon loss of elasticity in the lung, the retraction energy being compromised so that the expiratory phase which normally is passive must be assisted by muscular effort. During the day the patient throws the necessary muscles into play subconsciously, but during sleep the cortical centres fail to supply the necessary stimulation and this accounts for the frequency with which the patient is awakened from sleep in an attack of dyspnœa. The difficulty of expiring being the cause of the dyspnœa, expiration is evidently facilitated by the upright position because this is the posture that gives most relief to the patient. Hofbauer has studied the mechanism of this relief by careful *x*-ray examinations of the position of the diaphragm in various postures. Very unexpectedly he has found that the diaphragm is higher in position and its excursions far wider in the lying than in the sitting or standing position. This apparently contradictory finding Hofbauer explains thus: The lung has an adherent tendency to contract, and whenever the negative pressure in the pleural cavity is diminished, as by an accumulation of air or water, the lung assumes gradually the contracted state. This

tendency to contract is one of the chief factors in the expiratory phase, and the more distended the lung the more forcible will be the subsequent contractions. In pneumothorax, for instance, the dyspnœa is caused by the drawing of the mediastinum over into the unaffected side, thus hampering the dilatation of the normal lung. At operation, if the mediastinum be seized with forceps and drawn into the normal position, the dyspnœa stops at once. In a sitting posture similar conditions obtain. The low position of the diaphragm increases the capacity of the chest and holds the lung in a more distended condition so that the elastic expiratory recoil becomes more efficient. The dyspnœa being expiratory in type this renders breathing easier.

Tabes Dorsalis, Disease of the Circulatory Organs, and Syphilis.—Rogge and Miller (*Arch. f. klin. Med.*, 1907, lxxxix, 514). Although the association of tabes and disease of the circulatory organs, especially of aortic insufficiency and aneurysm, is well known, the frequency of the combination and its clinical importance has not been sufficiently emphasized. In 22 consecutive cases entering von Strumpell's clinic 8 showed definite signs of cardiac or arterial disease. This is probably an unusually high percentage, and the examination of the total clinical material gives the occurrence of definite organic heart or aortic disease as 10 per cent. Such a frequent association indicates that a common causative factor underlies both. In 24 selected cases in which the two diseases occur together Rogge and Miller find that disease of the aortic orifice is by far the most common complication, occurring in 15 instances. Aneurysm was present in 9 instances; never isolated, but in combination with other serious disease of the arterial system and most frequently with aortic insufficiency. The aneurysms were all fusiform, resembling the marked dilatation of the arch so commonly found in combination with the aortic insufficiency following arteriosclerosis. In several instances there were marked clinical signs of a pure myocarditis, and in others advanced arteriosclerosis at an early adult age—twenty-seven to thirty-five years. It is interesting to note that subjective symptoms were complained of in only about half the cases, the cardiac disease being discovered in the course of a routine examination. This suggests that many of the sudden deaths in tabes may be more closely related to disease of the circulatory apparatus than to degeneration of the bulbar centres. It emphasizes, too, how frequently the severe pains usually ascribed to purely nervous influences may have a real anatomical basis. Syphilis is the most important factor in the etiology, 9 cases giving a definite history and 10 more a very probable history. Other infectious diseases are not prominently present in the past history. Alcohol, tobacco, and hard work cannot be important factors, since there is a higher percentage of female patients of this selected group than in the whole number of tabetic cases. In the cases giving a definite history of syphilis there had been insufficient treatment after infection.

SURGERY.

UNDER THE CHARGE OF

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Cure of Hydrocele by Extraserous Transposition of the Testicle, after Incision, Retroversion, and Retrofunicular Suture of the Tunica Vaginalis.—GENOUVILLE and PERAIRE (*Annales des maladies des organes genito-urinaires*, 1907, xxv, 481) in a report of 45 cases calls attention to 4 cases in which the injection of iodine for the radical cure had failed. The injection in the first had caused an hematocele with the loss of the testicle; in the second it was followed by a recurrence; in the third there were three vaginal concentric pouches with a failure of the iodine to extend to all, and thus a failure; and in the fourth there was a hernial sac filled with a translucent liquid, besides a small vaginal hydrocele. The iodine was dangerous to the hernial sac and did not reach the hydrocele. Of the many operations for hydrocele, Genouville and Peraire consider the two most important to be, (*a*) excision of the sac and (*b*) retroversion and fixation of the sac. They have employed local anesthesia with cocaine in all their cases. For anesthesia of the testicle and vaginal tunic a concentrated solution of antipyrine was applied, which completely suppressed the sensibility of the testicle. After making the scrotal incision into the tunica vaginalis the testicle was isolated from below upward with a portion of the cord. The two edges of the tunic were then turned backward until they met behind the cord, where they were sutured together, beginning at the lower pole of the testicle, turned upward, and continuing the suture to the upper pole of the testicle, where the edges of the tunic were made to surround the cord closely. Not infrequently after this operation the vaginal tunic has folded on itself to form a new vaginal cavity and a new hydrocele. To avoid this the writers make a subcutaneous pouch to the internal side of the scrotal wound, in which the testicle is placed and where it contracts adhesions to the surrounding cellular tissue. The wound is then closed and a strongly compressive dressing applied. They have had no recurrences.

Hermetic Suture of the Bladder, by Detachment and Turning in of the Mucosa.—DELBET (*Annales des maladies des organes genito-urinaires*, 1907, xxv, 518) says that while an open wound of the bladder tends to close spontaneously, it does so slowly in many cases, and that the general tendency now is to close it primarily when there is no special contraindication. He is not inclined to accept the reports of some surgeons that primitive and total reunion is the ordinary result of their

operations. More frequently he believes a partial closure by cicatrization and a limited fistula is the result, with total closure later. In many cases the effort is a complete failure. The alteration from tension to flaccidity due to the filling and emptying of the bladder causes the edges of the wound at the time of tension to be slightly separated and urine to leak through. This happens in spite of the retained catheter, which is frequently blocked by clots of blood. A wound of the peritoneal surface closes as easily as a similar wound of the intestine. In default of the serous surface in extraperitoneal wounds, the mucosa is rich in bloodvessels and produces rapid cicatrization. Delbet closes a hypogastric extraperitoneal wound of the bladder as follows: The edges of the wound in the mucosa are caught with forceps, and with a bistoury or scissors the mucosa is separated from the muscularis around the wound for about 1 cm. With interrupted sutures or a continuous suture the muscularis is caught on both sides at the limits of the denudation, and at the time of tying them the edges of the mucosa are turned inward and their raw surfaces approximated. The internal hydrostatic pressure forces the raw surfaces closely together, rendering them water-tight. This method was employed in 2 cases with primary union in both.

A Contribution to the Study of Spontaneous Cure of Tuberculosis of the Kidney.—DESCHAMPS (*Annales des maladies des organes genito-urinaires*, 1907, xxv, 589) says that for some years the surgical therapy of renal tuberculosis has been the order of the day, and that the majority of surgeons consider that early radical operation, nephrectomy, is the only operation capable of producing a cure. Duhot, for instance, said that, potentially, renal tuberculosis may be spontaneously cured, but that no case has been demonstrated anatomically and that clinically it does not exist. Rafin said that the pseudocures are examples of either a total destruction of the kidney or an obliteration of the ureter which excludes the kidney from the rest of the organism. Deschamps says that renal tuberculosis, like tuberculosis elsewhere, can be cured spontaneously, and that to propose a nephrectomy at once when tubercle bacilli are found in the urine, is the same as to advise an amputation of the thigh for a white swelling of the knee. Besides, early removal of one kidney does not prevent tubercularization of the other. The indications for nephrectomy given by the writer are as follows: When the whole kidney is invaded by the tuberculous process and there is little or no parenchyma left; when there is a coincident existence of a pyonephrosis and signs of general infection; when hematuria is abundant and repeated; when the painful crises are frequent and when there is a progressive cachexia caused by tuberculosis of the kidney. He reports two cases of cure, in one of which a nephrectomy was done with drainage, and in the second case medical treatment and a trip to the country were followed by a complete cure.

A Case of Early Intervention for Severe Burn of the Stomach.—LAMBOTTE (*Jour. de chir. et annales de la Société Belge de chir.*, 1917, vii, 175) says that the ingestion of a caustic liquid produces, in a considerable proportion of cases, isolated lesions of the stomach wall, without involving the mouth or œsophagus. It may prove severe enough to be fatal. When the patient lives, two kinds of results may ensue: those occurring

in the days immediately following the accident, and the later results from cicatricial stenosis, which may appear some weeks or years after the burn. In Quenu and Petit's analysis of 94 cases, 59 with autopsy reports and 34 with operation, there was not a single case showing early operation, that is, in the first days after the operation.

March 1 last a young servant swallowed a considerable quantity of what is thought to have been commercial hydrochloric acid. Very severe pain in the abdomen and vomiting followed immediately and on the following day hematemesis. Ice was applied to the abdomen and the pain calmed by morphine. In the succeeding days vomiting became incessant, the pain continued to be acute, and the feeding was impossible. March 5, when Lambotte first saw the patient, the condition was very grave. The temperature was 38.6° C.; vomiting incessant, of fetid and brownish material; pulse rapid; abdomen very painful, tender, and rigid. There were no signs of burn of the mouth or œsophagus, but the lips were slightly ulcerated. Immediate operation was advised to remedy a menacing perforation and to permit feeding, and was performed an hour later. The pyloric half of the stomach was injected and thickened, and gave the sensation of a tumor on palpation. This tumor ceased abruptly at the pylorus and diminished insensibly toward the middle of the stomach. No trace of perforation was seen. Posterior gastro-enterostomy was performed, with a very large anastomotic opening. The gastric mucosa was absolutely necrosed, and detached itself in fetid and black shreds. On the following day the patient's condition was satisfactory. Diuresis was reëstablished and vomiting had ceased, and the general condition fairly good. After four days the patient became distinctly convalescent, and on the nineteenth day the cure was complete. Lambotte is convinced that without operation a fatal termination would have ensued.

Complete Rupture of the Left Kidney; Partial Nephrectomy; Cure.—Lambotte (*Jour. de chir. et annales de la Société Belge de chir.*, 1907, vii, 177) reports a case in which a boy, fifteen years old, fell his length on the pavement, striking his left kidney region on the edge of a stone. He had severe pain which rapidly subsided. It returned, however, and with it came an attack of mild syncope. He passed a small quantity of urine, with some blood in it. Rupture of the kidney was diagnosticated and he was taken to the hospital. When Lambotte saw him, six or seven hours after the accident, he found distinct rigidity, but a good general condition. An incision in the loin showed a large quantity of clotted and liquid blood. The kidney was rapidly delivered through the wound and found to be badly lacerated. The upper third of the organ was removed. The remaining lacerated portion was repaired by catgut sutures and ligatures, and the wound drained with guaze. The wound oozed abundantly at first, and later suppurated; but the final result was very satisfactory.

The Treatment of Joint Ankylosis by the Transplantation of Plates of Cartilage.—Weglowski (*Zentralbl. f. Chir.*, 1907, xxxiv, 481) says that, unfortunately, we are far from obtaining full function by our treatment of joint ankylosis, and that usually we purposely aim to

obtain an ankylosis in good position. Attempts to procure a movable joint have been made by placing between the joint surfaces foreign tissues, such as fasciæ, fatty tissue, muscle, or various foreign bodies like celluloid, gold plate, etc. Weglowski has employed plates of cartilage for this purpose on a case of elbow-joint ankylosis, upon which he had already operated unsuccessfully. The joint surfaces adhered together soon, in spite of the systematic employment of gymnastic exercises. He then concluded to try the transplantation of cartilage. After separating from the joint structures for a considerable area the soft tissues and periosteum, he sawed through the mass, at about the lower epiphysis of the humerus, with a Gigli saw set in an ordinary saw-frame. Then the upper end of the ulna was cut out, the head of the radius shelled out, and the remaining excess of bone was removed. He then exposed the cartilages of the sixth and seventh ribs, and removed two plates of cartilage together with the perichondrium in the whole length and breadth, but only half the thickness of the cartilages. These two pieces were then placed between the newly formed bony surfaces, the perichondrium being turned toward the epiphysis of the humerus. They did not require special means of attachment, since they were held in place by the adjacent bony surfaces. The wound was closed by suture throughout and a plaster cast was applied. After ten days the dressing and sutures were removed, showing healing by first intention. From this time on active and passive movements were carried out. In a month 60 to 70 degrees of flexion and extension could be performed easily, while pronation and extension were completely normal.

Unfortunately the patient died, five weeks after the operation, of pneumonia. This, however, permitted an examination of the joint operated on. The transplanted cartilage was found fixed firmly to the humerus. The apposed bony surfaces were smooth, even, and slightly glistening. Microscopic examinations showed new blood-vessels between the perichondrium and the bone. The cells and their nuclei of the cartilage stained with various stains.

Veronal-chloroform Narcosis.—Poktilo (*Zentralbl. f. Chir.*, 1907, xxxiv, 505) recommended this combination for general anesthesia in an article published two years ago. Since that time it has been employed in Professor Diakanow's clinic in Moscow, and has given entirely satisfactory results. The dangers of chloroform and ether may be met by decreasing the quantity or by using an antidote, especially for the evil effects of chloroform on the heart. This combination has the additional advantage of overcoming the effect of excitement of a nervous patient from the prospect of an approaching operation. It likewise lessens the quantity of chloroform necessary and diminishes the after-effects, such as headache, nausea, and vomiting. Veronal produces sleep without any evil effects, and causes the appearance in the urine of "amido" (NH_2), which, like ammonia, acts favorably on the heart. Given $1\frac{1}{2}$ to 2 hours before the operation, it will put the patient into a sound sleep or a partial sleep by the time he is brought into the operating room, so that he will be indifferent to the operation. A comparison was made between the effects of three combinations with chloroform, bromethyl-chloroform, hedonal-chloroform, and veronal-chloroform. The patient was anesthetized, on the average, with the first in 5.21 minutes,

with the second in 3.82 minutes, and with the third (veronal) in 2.58 minutes. Excitement was observed in the first in 45.08 per cent. of the cases, in the second in 27.17 per cent., and in the third (veronal) in 22.70 per cent. The average duration of the excitement was 2.89 min. in the first, 1.87 min. in the second, and 1.30 min. in the third (veronal). Vomiting was observed in 16.83 per cent. in the first, 6.79 per cent. in the second, and in 2.30 per cent. in the third (veronal). Asphyxia occurred in 7.62 per cent. in the first, 4.53 per cent. in the second, and 1.15 per cent. in the third (veronal). In one minute on the average there was consumed, in the first 0.69 c.c., in the second 0.57 c.c., and in the third (veronal) 0.61 c.c. The relatively better results from the veronal-chloroform combination deserves that it be further employed and its effect carefully noted.

The Technique of Intestinal Suture.—SCHOEMAKER (*Zentralbl. f. Chir.*, 1907, xxxiv, 508) considers, from his experiments on dogs, that the end-to-end union of divided intestine with circular suture gives better results than the end-to-side or the side-to-side or lateral anastomosis, and that it should, therefore, be preferred in men. Intestinal resection is the more dangerous the more complicated the suture employed. The chief difficulty met with is in closing properly the interval between the two layers of peritoneum of the mesentery where it is attached to the bowel. Schoemaker's method is as follows: These two layers of peritoneum slightly separated near the gut, corresponding to each divided end of the intestine, are brought together and turned in as when the intestinal end is to be closed, by two sutures. On one side the threads are cut close to the knot, and on the other side are left long, without regard to the rest of the divided mesentery. One long end of the suture nearest to the bowel is then employed as a circular suture to unite the two ends of the intestine. This suture is made to catch the serous, muscular, and submucous coats or all the coats, and when it completes the circumference of the bowel it is knotted to the other long end of the same suture and cut short. The second suture, that farthest away from the bowel, is similarly used as a circular suture, including only the serous coat, and thus covering in the first suture. Schoemaker employed this method in 10 cases without a failure. It is not so successful in uniting the divided ends of the large intestine, since the non-peritoneal surface of this bowel is larger and the edges of peritoneum too far apart.

Stab Wounds of the Heart.—HARTE (*Annals of Surgery*, 1907, xlv, 672) says that the consensus of opinion among experimenters is that the heart after being exposed can be grasped with the hands or forceps and gently compressed with no appreciable effect on its action; that punctures with needle or knife produce only a temporary irregularity in the heart's action; that wounds produced during systole bleed more than those occurring during diastole; that wounds of the ventricle produced during systole are larger than those produced during diastole; that oblique wounds bleed more than perpendicular wounds; that wounds of the right ventricle are more dangerous, because of the thin ventricular wall and because blood in the right heart coagulates more slowly; that wounds of the heart heal kindly, and that the cicatrix is complete

in two weeks; that interrupted sutures are better than continuous ones; that the material enclosed in the grasp of the sutures causes atrophy and is replaced by scar tissue; that superficial stitches are less likely to tear out than deeper ones, and that the stitches should be inserted and tied during diastole, because of the danger of tearing out during systole.

Fisher, after an analysis of 452 heart wounds, says that from 7 to 10 per cent. recover spontaneously. Harte thinks this estimate high, but considers that even if it were positive it should not deter one from prompt surgical interference if the condition of the patient warrants it. He believes that an anesthetic is imperative and that ether is preferable. The best suture material is chromicized catgut, reasonably fine, introduced on a sharply curved needle. In ventricular wounds the suture should be inserted deeply, even to entering the endocardium, as only by this method can accurate approximation be procured. In auricular wounds through-and-through sutures are imperative to prevent bleeding through the wound. The pericardium should be closed without drainage, the pleura with drainage in a dependent part of the chest. Harte reports a case in which a stab wound of the left auricle was sutured. The patient died twenty-four days after the operation, from infection of the pleural cavity, which was opened by the original stab wound.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Duration of Immunity following the Prophylactic use of Diphtheria Antitoxin.—STILLER (*Jahrb. f. Kinderheilk.*, 1907, lxiv, 442) from a year's observations at the Strasburg Children's Clinic concludes that prophylactic immunization lasts from three to five weeks provided the subjects are removed from infectious surroundings. If immunized children are subjected to possible infection, the immunity is naturally of shorter duration—ten to fourteen days for example. Children living in these surroundings are far more prone to contract the disease than those to whom antitoxin has been administered. Catarrhal affections and traumatisms of the mucous membranes predispose to infection and shorten the duration of immunity. Scarlatiniform eruptions which appear without fever or throat lesions, Stiller considers to be the manifestation of true scarlatina, a conclusion which hardly seems justifiable.

Radiotherapy in Leukemia.—VAQUEZ (*Revue française de médecine et de chir.*, 1907, v, 4) states that radiotherapy is our best means of combating the course of leukemia. It is without effect in the acute forms of the affection, but in the subacute and chronic types it may hold the disease in arrest. Radiotherapy is to be considered as a symptomatic measure only and has given no proofs that it is a cure; its injudicious employment, on the other hand, may be followed by grave results to the patient. It should be administered only up to the point of disappearance of the pathological modifications of the blood, to the exclusion of leukopenia. Every relapse should, upon its appearance, receive the same treatment as was given the disease originally. Methodical examination of the blood should be carried out in making the diagnosis, in following the course of the treatment during the active period of the disease, and in anticipating the occurrence of relapses.

Digitalis and Digitalin.—HUCHARD (*Revue de thérap.*, lxxiii, 24, 838) protests against the use of substitutes for crystallized digitalin. He states that it is not true that the infusion of digitalis leaves is preferable to the glucoside from a point of view of diuresis, for the latter possesses this effect to the same degree as the former. Digitalis varies greatly, depending upon its origin, the soil in which it grows, the method of the preservation of the leaves, etc.; all these render any accurate test of its action impossible. Consequently, a product of uniform strength is always preferable. The slowness of the drug's action can hardly be considered a fault; diuresis follows its administration in from twelve to forty-eight hours while cardiac stimulation takes place in fifteen minutes; these two effects are absolutely unconnected. It must be remembered that digitalin is diuretic only when œdema is present. The drug is not dangerous when properly employed, its action is lasting and its administration may be continued for months. 5 minims of a 1 to 1000 solution may be given daily as a cardiac tonic for long periods. Its elimination is retarded when the patient is kept in bed. The dose varies with the mode of employment and the indications; 50 minims of a 1 to 1000 solution during the day have a diuretic effect and may be repeated after eight or ten days if necessary. If such a dose is followed by a disappearance of the œdema the drug may be continued as a heart tonic in the doses indicated above. Digitalin may be given hypodermically in oily solution if there is likelihood of causing gastric disturbance.

Practical Value of the Opsonic Index in the Treatment of Disease.—CRACE-CALVERT (*The Lancet*, 1907, 1, 279) states that in ordinary sanatorium patients suffering from tuberculous disease of subacute type and whose progress is not what we should reasonably expect, inoculations of tuberculin, controlled by the opsonic index, may do a considerable amount of good. In such patients there is probably an absence of stimulus to the immunizing machinery and there is accordingly no corresponding production of antitoxins. If, now, by inoculating, the necessary stimulus is given a corresponding production of antitoxins, accompanied by a rise of the opsonic index and an improvement in the lung condition, should be evidenced. The index, however, does not always respond, for the author in one instance has observed a fair

amount of improvement in the pulmonary condition without much effect on the opsonic index. The appropriate doses of vaccine for a given patient can be learned only by experiment and repeated estimations of the index, but it has been proved that the doses ($\frac{1}{500}$ of a milligram and upward) recommended in the directions given with Koch's tuberculin are too large and better results can be obtained with smaller dosage. The dose generally employed by the author is $\frac{1}{1000}$ of a milligram. The frequency of the inoculations depends upon the length of time that the positive phase, following inoculations, lasts. At first the injections are usually given at seven to ten-day intervals, while, as the number of inoculations increases, the frequency is diminished until a positive phase lasting two months after an inoculation of $\frac{1}{800}$ of a milligram, may be noted.

The Effect of Amyl Nitrite Inhalations upon the Blood Pressure.—HEWLETT (*Jour. Med. Research*, 1907, xv, 383) after experimentation states that amyl nitrite increases the total output of blood from the heart both during the primary fall of systolic pressure and during the secondary rise. During the former the increased out-put is due to the more rapid heart action, during the latter mainly to a greater amount of blood expelled at each systole. It would consequently appear that though the drug dilates the peripheral vessels it does not necessarily reduce the blood pressure to a like degree. The latter is avoided by an increased output of blood from the heart. The typical action of amyl nitrite is not that usually ascribed to it, viz., dilatation of the peripheral arteries and fall of blood pressure. It does, indeed, dilate the bloodvessels, but it also causes the heart to pump more blood and the result is a more rapid flow of blood through the body. With regard to variations from the typical action of the drug the author has observed that the pulse rate in old persons, whose hearts are comparatively free from vagus control, does not become as accelerated after an amyl nitrite inhalation as it does in the young. In discussing the action of glyceryl nitrate Hewlett has observed, in patients who received a daily dosage of from 5 to 30 drops of a 1 per cent. solution, that following such dosage only a slight and inconstant effect on the blood pressure occurs. No great fall resulted, indeed, the systolic pressure rose about as frequently as it fell. When this drug causes the pulse to become "fuller and more bounding" Hewlett is inclined to believe that we are dealing with an effect similar to that of amyl nitrite. The action of glyceryl nitrate in relieving certain headaches and in reducing the number of attacks of angina pectoris is not simple, and it is possible that its effects in these conditions are not due to a resulting lessening of blood pressure but to an increased circulation of the blood.

Methylthionine Hydrochloride in Mercurial Stomatitis.—LAMOUREUX (*La Semaine médicale*, 1907, xxvi, 586) has used this agent in mercurial stomatitis as follows: Once a day, preferably in the morning, he applies powdered methylthionine hydrochloride to the ulcerations of the mucous membrane by means of a cotton swab. The mouth is then rinsed with a 2 per cent. solution of potassium chlorate; the latter procedure is repeated several times during the day. Of 6 patients thus treated 4

were cured by the fourth day, while the other 2 recovered within eight days. It is interesting to note that, in instances in which mercurial treatment must be energetically carried out, it need not be intermitted if this treatment of the stomatitis is employed.

The Treatment of Whooping-cough.—BLACHE (*Journal de médecine de Paris*, 1906, xviii, 512) recommends the following: Syrup of tolu, syrup of senega, syrup of eucalyptus, equal parts; dose 4 to 8 drams daily. During the convulsive stage the patient is given small frequent meals, after the third of which one or two spoonsful of black, sweetened coffee, which is held to be an excellent anti-emetic, are taken. During the catarrhal stage ipecac may be prescribed; this drug is most efficacious when the bronchitis is but slight.

Belladonna gives variant results. Blache employs it thus for patients less than one year old: Belladonna extract $\frac{1}{6}$ grain, powdered belladonna root 4 grains, sugar 8 grains. Mix and divide into twenty-five powders. From one to four of these should be given daily, the number being increased progressively. Children of from two to five years may receive six to eight powders per day. Good results may also be obtained by a combination of belladonna with potassium, sodium, or ammonium bromide in syrup. Drosera will also diminish the number and intensity of the paroxysms when given as follows: Tincture of drosera 40 parts, tincture of aconite 10 parts, tincture of belladonna 8 parts. Dose 20 to 50 minims daily, divided into 3 doses. Change of climate and air-baths are excellent means of hastening recovery.

The Prevention or Scarlatinal Nephritis.—THOMPSON (*Edinburgh Med. Jour.*, 1907, xxi, 103) states in regard to the use of a prophylactic drug against the nephritis of scarlatina that urotropin is the only one which has proved itself of value. Of 47 consecutive patients treated with this agent by the author not one had nephritis and only one exhibited albuminuria. These facts he considers encouraging enough to suggest the further use of the drug in scarlatina. Patients treated with hexamethylenetetramine were less fortunate in escaping nephritis, and he holds this drug to be not an exact equivalent of urotropin when considered from the point of therapeutic results. In conclusion, he suggests that all instances of scarlatina be treated from the beginning with 5 grain doses of urotropin three times a day for children up to twelve years; for patients above this age $7\frac{1}{2}$ grains thrice daily are advised. Generous dilution of the drug with water is necessary and the treatment should be continued to the end of the twenty-eighth day of the disease.

The Trypsin Treatment of Cancer.—LUTHER (*New York Medical Journal*, 1907, lxxxv, 341) states that the consensus of opinion of all those who have applied the treatment is that whatever else it may do, it certainly does, in most cases, cause: (1) An arrest or shrinkage of the growth; (2) improvement in the general nutrition in which the appetite is increased and the weight is maintained or augmented; (3) diminution or cessation of pain; (4) diminution in discharge with a decrease of fœtor; except in patients in whom sloughing occurs. In conclusion Luther emphasizes the fact that large doses (75 minims of a sterilized glycerin extract of freshly macerated pancreatic gland) are required

in order to obtain the best effects. The agent is administered hypodermically, and the injections may be given anywhere except into the tumor. They should be thrown deep into the cellular tissue but not into the muscular substance. Thorough asepsis should be observed and the syringe should be cooled after being boiled, for heat precipitates the trypsin.

The Treatment of Subacute and Chronic Gout.—LUFF (*Practitioner*, 1907, lxxviii, 161) states that in the subacute and chronic forms of gout, in addition to colchicum, which may be given in small doses, guaiacum is often useful as an alterative; here it stimulates the liver and affords relief to the portal system. It is given in the form of the resin in doses of 5 to 10 grains, two or three times a day, according to the effect on the bowels. In chronic gout the colchicine pill may be given three times daily. To encourage elimination through the kidneys, diuretics, such as potassium citrate or bicarbonate should be prescribed and water should be freely drunk. The citrate is the best potassium salt to combine with colchicum. It diminishes the acidity of the urine and increases the solvent power of this fluid for the uric acid salts. Mineral waters containing sodium salts are useful if the liver is sluggish, and, when there is gastro-intestinal catarrh, torpor or gouty dyspepsia. The lithium salts are less useful than those of potassium or sodium. The former may cause cardiac depression or even dilatation if they are taken in excessive amount. In order to lessen the articular thickenings and enlargements, the gouty pain in the side of the foot and gouty neuralgia, the internal administration of potassium iodide is advised. Its dosage should be 10 grains three times a day for six to eight weeks, and it is best given in a decoction of sarsaparilla.

PEDIATRICS.

UNDER THE CHARGE OF

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A Urinary Sign of Helminthiasis.—IEFIMOV (*Bull. méd.*, abstracted in *Revue des maladies de l'enfance*, January, 1907, p. 45) describes a urinary reaction which indicates, without fail, he states, the presence of intestinal worms: 5 to 10 c.c. of urine is received directly in a test tube, and without filtering (at least if not markedly turbid) is heated to boiling, and then 5 to 10 drops of the officinal solution of acid nitrate of mercury is added. In negative cases the urine becomes cloudy, lactescent, and throws down a white precipitate. In cases of helminthiasis this turbidity, as well as the precipitate, always takes on a grayish or even blackish tinge, due presumably to the presence of a toxin elaborated by the parasite, which is absorbed by the blood and finally eliminated by the urine. To ensure the accuracy of the test it is indis-

pensable that the subject shall not have recently taken certain drugs, especially alkalies, compounds of sulphur (including Dover's powder, which contains the sulphate of potash), certain iron preparations, and lead compounds, all of which give with the acid nitrate of mercury a grayish or blackish precipitate. This is not the case, however, with morphine, the salicylates, carbolic acid, salts of zinc and copper, phenacetin, quinine, and antipyrin. Purulent urine alters the reaction, but the presence of albumin, sugar, or indican does not interfere with it. This reaction is said to be produced by the presence of teniæ as well as of round worms. The grayish coloration of the precipitate is always more marked in the case of the tape-worm, but the difference is not sufficiently distinct to indicate the variety of the parasite. The differential diagnosis, however, can be made, according to Iéfimov, by a microscopic examination of the crystals obtained by evaporation of a thin film of the urine upon a glass slide. In the case of tape-worms there are a number of granular crystals; in the presence of nematodes, star-shaped crystals are found, which are particularly large and beautiful when ascarides are present in the bowel.

OBSTETRICS.

UNDER THE CHARGE OF

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The Results of Active Interference in the Treatment of Parturient and Puerperal Cases.—HOFMEIER (*Monats. f. Geb. u. Gyn.*, 1906, xxiv, Heft 4) discusses this important subject at length. 3.3 per cent. of the children are stillborn. Of these, 1.9 per cent. perish during labor. These cases may be divided into two classes: First, those where the bony pelvis occasioned no complication in labor; and second, those in which contraction of the pelvis, with or without other complications, brought about the result. In the first group are 56.6 per cent. and in the second, 43.3 per cent. of cases. During labor 16 per cent. of the children born in contracted pelves perished. This mortality has been decreased of late years by operations increasing the size of the pelvis and by Cesarean section. The infant mortality of induced labor is very unsatisfactory. Krönig estimates that among 440 labors, 2.5 per cent. terminated in fetal death. When interference was practiced in labor, fœtal mortality arose to 20 per cent., and during forceps extraction was 12 per cent. Hofmeier's figures show 10 and 2.5 per cent. respectively in the Würzburg clinic. Among eleven children delivered by pubiotomy and Cesarean section, 9 per cent. perished. In the Würzburg clinic, 66.6 per cent. of labors in contracted pelves, terminated spontaneously; 33.4 per cent. required interference of some sort. Among these patients 26 per cent. of the children perished, but this occurred in cases which were not treated by Cesarean section, or operations for enlarging the pelvis. Maternal mortality in cases in which the children perished during labor

is usually very small. In 163 cases in which interference other than Cesarean section or pubiotomy was practised, no mother died. n 27 cases in which operation was undertaken in the interests of the children as well as the mother, 3 died—one after symphysiotomy, one after pubiotomy, one after Cesarean se tion.

Care of the Perineum and Pelvic Floor.—APFELSTEDT (*Berl. klin. Woch.*, November 26, 1906) endeavors to prevent injury to the perineum during labor by placing the patient upon the back with the thighs widely separated. The left hand supports the perineum with four fingers, the forearm being supported upon the bed. Two fingers are placed upon each side of the coccyx. The fingers of the right hand are pressed between the occiput and the pubes, controlling the exit of the head. Unless the patient is controlled by anesthesia at the moment of birth, she is asked to count when strong expulsive pains come on, thus reducing the danger of laceration by strong voluntary expulsive efforts. Should a tear occur, a curved needle is passed deeply into the torn muscular tissue from the centre of the wound close to the margin. This is carried out on both sides, a heart-shaped suture being passed and buried.

Labor Obstructed by Osteosarcoma of the Pelvis.—RAY (*Brit. Med. Jour.*, January 26, 1907) reports the case of a patient who gave birth to a child eighteen months before coming under observation. During the present pregnancy she had suffered from pain in the hips and on examination was found to have lost weight and to be very costive. When labor developed, a tumor was found near the sacrum as large as a child's head. Under ether an incision was made and a tumor found, smooth, tense, and elastic. The tumor was opened and found to be not fluid, but solid. Its removal could not be effected. Two hours after operation the patient had bleeding, and labor gradually developed. This was terminated by the delivery of a dead child by version. The child was stillborn, and the mother also perished shortly afterward. On examination, the tumor was found to be an osteosarcoma of the sacrum and coccyx.

The Influence of Meat Diet upon Fertility and upon Lactation.—WATSON (*Brit. Med. Jour.*, January 26, 1907) has experimented upon rats, some of which were fed upon meat and the others upon milk. Those fed upon meat remained sterile, while those fed upon milk conceived and were able to nourish their young.

Postpartum Hemorrhage.—LE PAGE (*Brit. Med. Jour.*, January 26, 1907) has treated postpartum hemorrhage successfully by the following method: The patient's pelvis is raised considerably. The abdominal aorta is compressed against the bodies of the vertebræ; the legs and arms were held up and bandaged. The hand was made thoroughly aseptic, introduced within the uterus, and clots removed. Ergot was administered, and brandy and water injected into the rectum. The pressure upon the aorta was continued, and very gradually removed. Care was taken also to remove the bandages from the legs and arms very gradually.

Cesarean Section for Contracted Pelvis Complicated by Twin Pregnancy.—COWEN (*Brit. Med. Jour.*, January 26, 1907) reports the case of a primipara, aged thirty-five years, with a rachitic pelvis, whose true conjugate was about three and one-third inches. As it was impossible to deliver the children through the vagina, they were extracted by abdominal incision. At the request of the parents, to prevent further conception, the Fallopian tubes were also excised. There were two placentæ which occupied the greater portion of the uterine cavity. Mother and children recovered.

Scopolamine and Morphine to Produce Analgesia during Labor.—In the report of the proceedings of the Obstetrical Society of Berlin (*Zeitschr. f. Geburtshülfe und Gynäk.*, 1907, Band lix, Heft 1) HOCHEISEN quotes Viron and Morel as reporting 2000 cases of this anesthesia, with 25 deaths; Roith, 4000 cases with 18 deaths; Wartapetian, 50 per cent. of the children asphyxiated; and Gauss, in Krönig's clinic, 500 cases with good results. Hocheisen and Bardeleben report between 120 and 130 cases. The drug produced an apparently light sleep, from which the patient was aroused. Gauss had good results in 76 per cent. of his cases. Hocheisen and Bardeleben had negative results in 18 per cent., and the influence upon the patient produced by the drug did not seem to be in proportion to the dose. In 65 per cent. the desired light narcosis was obtained. Very decided after-effects, as redness about the head, thirst, and rapid pulse, were observed in 70 per cent. of cases. The physician must not leave the patient while under the influence of the drug, as unpleasant symptoms often develop. Uterine contractions were observed in a considerable number of cases. In 24 per cent. abdominal pressure was distinctly lessened. The application of forceps was necessary in 25 per cent. of cases. The length of labor was increased. Postpartum hemorrhage was more frequent, 1 case proving fatal, and the time occupied in the delivery of the placenta was longer than normal. The puerperal period was also complicated by subinvolution. After labor, 1 patient had severe disturbance of the heart and seemed to be in great danger of heart failure for several hours. In 20 per cent. of the cases there was slowness of the pulse and intermittent beat. The action of the heart and the respirations were disturbed in many of the children. One fatal case was observed, which seemed fairly to be ascribed to the drug given. In the discussion of this report, Gauss agreed in the dangers of the method, and Bumm thought that the method was not suitable for general practice.

What is the Exciting Cause of Labor?—This interesting question receives considerable attention by SCHATZ (*Archiv f. Gynäk.*, 1906, Band lxxx, Heft 3), who believes that the phenomena of menstruation and labor depend upon rhythmical variations, producing a maximum and minimum in blood pressure. The tendency is to divide the various periods of the mouth into halves. Especially is this true in the last three half-months of pregnancy, and in the month extending from January 19 to February 18, thence to the week of confinement, or even the half-week preceding. The physiological week is not a primary division of the physiological month. Periodic activity in the bodily functions seems to have a definite relation by division in multiples of two. The physio-

logical week is one step in the subdivision of the physiological month. A short month would be twenty-one days between menstruation, usually divided into four periods. The more early and complete the division of the month's curve of blood pressure, the greater the liability in the regularity of the periods of the given patient. When these variations become excessively frequent, the intervals being minutely divided, it is considered a sign of what the author terms "angioneurasthenia." Lack of this excess of division is characteristic of a well-balanced vasomotor nervous system. The illustration of this theory is observed in a case of epilepsy. When conception occurs a new periodicity begins. An effort may be made to predict the time of confinement by studying the blood curve of the patient. Labor is most apt to take place during the period of increased blood pressure, and as this varies in different patients it is obvious that each case must be studied individually, to attempt a prediction.

The Secretion of Sweat from the Axillary Glands Resembling Milk, and Occurring during the Puerperal Stage.—SEITZ from the clinic at Munich (*Archiv f. Gynäk.*, 1906, Band lxxx, Heft 3) reports two cases of this unusual abnormality. From the second to the fourth day of the puerperal period these patients complained of pain in the axillary region, with sweating on both sides beneath the skin. The tissues seemed to be infiltrated, the veins engorged, and the whole axilla filled, but without redness. On pressure sweat exuded from the axillary region. Microscopically this fluid closely resembled milk. These cases were not polymastia in the axillary region. There were no nipples or mammary glands developed, and the fluid could definitely be recognized as sweat.

Placenta Circumvalata and Marginata.—LIEPMANN (*Archiv f. Gynäk.*, 1906, Band lxxx, Heft 3) considers this condition as caused by defective development in the membranes. Placenta marginata develops from placenta circumvalata. It is probable that a condition of endometritis precedes these abnormalities, and that the infarcts which form are secondary to defects in the membranes. These abnormalities are the result of an unusual location of the placenta, or some abnormality in the amniotic liquid, or in uterine contractions occurring during pregnancy. The condition clinically is not of importance as regards the third stage of labor.

GYNECOLOGY.

UNDER THE CHARGE OF

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Medical Treatment of Uterine Hemorrhage.—AARONS (*Brit. Gyn. Jour.*, 1907, No. 2), in a paper on this subject, presents a series of 93 cases in which various drugs were used before resorting to curettement.

He emphasizes the importance of ascertaining the cause of the bleeding before resorting to any treatment. He found a combination of ergotin, cannabina tannate, hydrastin, and stypticin especially useful. Styptol, ¾ to 2 grains three or four times daily, checked hemorrhage in all but two cases in which it was used. Aarons thinks that it neither produces uterine contractions nor does it act on the vasomotor system. Calcium chloride was particularly useful, by increasing coagulability of the blood, especially in cases of fibroid tumors. No styptic applications to the interior of the uterus were made except after curettement.

In several instances hemorrhage was checked by rectal injections of sterilized gelatin, given three times daily, according to Lancereaux's suggestion with regard to treating aneurysm by causing coagulation of the blood. Hot douches were rarely used.

Conservative Treatment of Inflammatory Diseases of the Adnexa.—HAERRMANN (*Münch. med. Woch.*, 1907, p. 145) reports 1244 cases from the Munich Clinic, in only 20 of which were the organs extirpated. He infers that operations may be necessary in cases of acute inflammations of the tubes and ovaries and pelvic connective tissue in which life is endangered. In all cases of tuberculosis a radical operation should be performed; also when conservative treatment has been tried without benefit. In only 7 out of 180 cases was such surgical treatment necessary. Although gonorrhea was inferred to be the cause of disease in the majority of the cases, the pus evacuated was nearly always sterile; gonococci were seldom present, streptococci more frequently. Intestinal infection was thought to be the cause of the adnexal disease in several instances. Haerrmann lays considerable stress on the blood count as an aid to the diagnosis of suppurative processes. The conservative treatment included the pressure and hot-air methods; massage was rarely used and electricity never. Absolute rest in bed, hot douches, and tampons were employed as routine measures. The average stay of the patients in the hospital varied in different kinds of cases from 37.3 to 55.7 days. In only 36 cases was vaginal section necessary in order to evacuate pus.

Intestinal Obstruction due to Parametritis.—KULIGA (*Monat. f. Geb. u. Gyn.*, vol. xxiv, 1906, p. 598) reports 3 cases in which exudates caused almost complete occlusion of the rectum and subsequently intestinal paralysis. He cautions against treatment by heat and pressure, which cause fresh inflammation, and also points out the danger of perforating the wall of the gut with the long rectal tube. He advises that an artificial anus should be made instead of operating directly for the obstruction.

Fusion of an Ovarian Cystoma with the Uterus.—MEYER (*Zentralbl. f. Gyn.*, 1906, No. 44, p. 1239) reports a case in which the uterine wall was partially transformed into a multilocular cyst, which seemed to originate in the uterus itself. The well-defined line of separation between the uterine muscle and the neoplasm and the fact that the exterior of the cyst was covered in several spots with serous epithelium showed that it was really of ovarian origin and had invaded the uterus secondarily. The lining membrane of the cystoma consisted of columnar

epithelium secreting mucus, which resembled closely that of the intestine and thus suggested that the neoplasm was doubtless a teratoma of the ovary.

Results of Vaginal Extirpation of the Cancerous Uterus.—Blau (*Beiträge zur Geb. u. Gyn.*, Band x, Heft 3) presents the statistics of Chrobak's clinic from 1890 to 1893. Of the cases of cancer of the uterus 20.46 per cent. were regarded as operable, 18.5 per cent. being suitable for vaginal hysterectomy. There were 309 cases of vaginal extirpation (87.7 per cent. for cancer of the cervix and 11.65 per cent. for malignant disease of the corpus uteri), the primary mortality being only 5.8 per cent; 244 patients have been kept under observation, 161 of whom were regarded as promising a favorable result. Of the latter 30.4 per cent. are still free from recurrence. The proportion of absolute cures has been estimated by Winter as only 5.64 per cent.

There were 113 cases of igni-extirpation (in 47 of which Schuchardt's incision was employed), with a mortality of 6.19 per cent., the proportion of those permanently cured being 45.8 per cent. (Such remarkable results as these obtained by so reliable an observer as Chrobak must impress American gynecologists not only with mixed envy and admiration, but with a mournful sense of the small number of operable cases which are submitted to them as compared with the proportion in German clinics. This unfortunate condition is due directly to the fact that neither the profession nor the laity in this country has yet learned to recognize the early signs of malignant disease of the uterus.—H. C. C.)

Papillary Tumors of the Ovary.—Estor (*Gaz. des hôp.; Zentralbl. f. Gyn.*, 1906, No. 44, p. 1242) admits that the etiology of these neoplasms is unknown. He distinguishes a benign and a malignant variety, the latter developing in younger subjects, but both between the ages of forty and forty-five. The former may remain benign for a long time, then may suddenly undergo malignant degeneration and form metastases.

Both ovaries are nearly always affected and ascites is a common accompaniment, while adhesions, metastases, disturbances of the intestinal tract and of menstruation are usually present. Papillary cystomas may exist for several years before the patient succumbs, and the prognosis is favorable even after an incomplete operation (?). As regards operative treatment Estor recommends total extirpation of the uterus with the cysts if evidences of malignancy are noted; otherwise, supravaginal amputation. When ascites exists drainage should be maintained for three or four days. The primary mortality is high—in Estor's cases 15 per cent. (It would seem as if he failed to distinguish clearly between benign and malignant neoplasms, especially with regard to the indications for radical operation. It is important clinically to note that there is a wide difference between true metastases and papillary growths found in the peritoneum in cases of non-malignant cystomas.—H. C. C.)

Infection of Ovarian Cyst with Eberth's Bacillus.—Bensis (*Orient. méd.; Zentralbl. f. Gyn.*, 1906, No. 44, p. 1243) reports the case of a patient, aged forty years, who had had an ovarian cyst for sixteen months

which was mistaken for pregnancy. Two and one-half months before entering the hospital she had typhoid fever, during the course of which the tumor rapidly increased in size. Purulent fluid removed from it with an aspirator contained Eberth's bacilli. The temperature was normal. The patient's condition was such that a radical operation was impossible. Twelve pounds of pus was removed with a trocar, but the patient died a few hours later.

Cysts of the Tubal Mucosa.—CORNIL (*Bull. et mém. de la Soc. anat. de Paris; Zentralbl. f. Gyn.*, 1906, No. 44, p. 1244) removed a cystic ovary with a tube the size of the thumb. The ovary was a unilocular cyst with papillary growths on its inner wall, covered with columnar epithelium. The mucous membrane of the tube contained many small submucous cysts, which appeared to be deep depressions of the mucosa, covered with cylindrical epithelium and surrounded by connective tissue. Cornil thinks that this condition must be rare, as it has not been previously described.

Intraligamentary Cysts.—SJANOSZEWSKI (*St. Petersburg Dissert.; Abst. in Zentralbl. f. Gyn.*, 1906, No. 44, p. 1244), from an analysis of nearly 500 cases, concludes that it is impossible to define exactly the point of origin of these neoplasms, whether the ovary, parovarium, or broad ligament. They usually develop between the ages of twenty-five and thirty-five years, and in 36 per cent. in nulliparæ.

The general primary mortality after operation is 10.9 per cent., due to frequent adhesions, injury to the hollow viscera, and the escape of infected cyst fluids. Subsequent exudations are common and result in a mortality of 2.5 per cent.

Colpotomy is the preferable operation, being easier, attended with less risk of traumatism than laparotomy, a shorter period of convalescence, and fewer subsequent complications. The vaginal route is especially convenient for the removal of suppurating cysts, as the peritoneal cavity is not invaded; partial removal of the sac with drainage is best accomplished per vaginam.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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Intranasal Origin of Epilepsy.—HEYNINX, of Brussels (*Archives internat. de laryng., d'otol., et de rhin.*, March–April, 1906), reports four cases in support of his contention that inflammatory reaction at the vault of the nose and in the subcranial sinuses may be the cause of

epileptic seizures in consequence of the retention of septic secretions due to hypertrophic and congestive compression of the subjacent tissues, and especially the middle turbinate.

Nasal Disease a Main Cause of Facial Erysipelas.—CULLEN F. WELTY (*Jour. Amer. Med. Assoc.*, December 22, 1906) contends that so-called idiopathic erysipelas is a misnomer. He states that 82 per cent. of cases of facial erysipelas start from the angle of the nose and are due to direct infection from a contaminated field of pure or mixed infections of streptococci, which can be substantiated in the majority of instances. These views were confirmed in a discussion.

Transformation of Nasal Mucous Polyps into a Melanotic Tumor.—GEORGES PAUTET (*Revue hebd. de laryng., d'otol., et de rhin.*, December 1, 1906) reports a case in which he was enabled to follow the slow evolution of transformation of a mucous polyp of the nose into adenoma and finally into melanosarcoma. This occurred in a man fifty-two years of age, who first came under observation September 13, 1900, and, after a number of surgical procedures at varying intervals, eventually died in cachexia on May 10, 1904.

Operations on a Denuded Nasal Septum.—E. ESCAT (*Revue hebd. de laryng., d'otol., et de rhin.*, November 3, 1906) reports and illustrates one case in which he gained access to the septum by cutaneous incision between the lip and the point of the nose, followed by denudation of the cartilage and its removal with simple scissors. The cutaneous incision was united with sutures which were removed on the fourth day. Three months later both the physiological and esthetic conditions were excellent.

Turbinectomy.—E. HARRISON GRIFFIN (*Med. Record*, April 14, 1906) states that he has operated so far on more than ten thousand cases without having seen one in which the result was not most gratifying, and the aim of the operation secured—perfect nasal breathing and a drain for the nose and all the sinuses that empty into the nostril. He removes only enough of the bone to establish drainage and to avoid the possibility of contact with the septum, finding it unnecessary to remove the entire hypertrophied bone. Before operating, he administers quinine and potassium bromide for one to two weeks to reduce congestion and diminish risks in hemorrhage. In operating he uses a saw, with the aid of forceps, snare, and scissors, utilizing cocaine anesthesia, but avoiding adrenalin.

Pemphigus of the Mouth and Pharynx.—M. HECHT (*Revue hebd. de laryng., d'otol., et de rhin.*, October 20, 1906) reports the case of a man, aged forty-four years, who for six months had an affection of the buccal and pharyngeal mucous membranes, manifested by the almost daily appearance of multiple yellow vesicles of the average size of a pea, which ruptured rapidly, leaving painful losses of substance. It extended at times to the epiglottis and to the arytenoid region, and had resisted all medication up to the time of presentation. On account of the absence of fever at each eruption, and the lack of manifestation in the skin, objection was taken to the diagnosis in the discussion which followed.

Adenocarcinoma of the Turbinates.—FIOCRE (*Revue hebd. de laryng., d'otol., et de rhin.*, October 20, 1906) reports a case of adenocarcinoma of the nose in a woman, aged sixty-three years, who complained simply of dulness of hearing, and was unaware that her right nasal fossa was occluded with a growth. This was removed, principally in one sitting, and a month later the passage seemed entirely clear, cicatrization being nearly complete, and nothing discoverable but healthy tissue covered with normal mucous membrane. The tumor occupied the position of the middle and inferior turbinates without invasion of any of the adjoining tissues, and had begun to undergo myxomatous degeneration.

Diseases of the Accessory Sinuses in Ophthalmic Affections.—HASTINGS (*Annals of Otol., Rhin., and Laryng.*, September 1906) discusses the subject, and reports a number of illustrative cases in point. He enumerates six ocular conditions other than orbital abscesses, as those most frequently met with in this connection, namely: Œdema of the eyelids, congestion of the conjunctiva, ptosis, squint, pain in the eye, and disturbance of vision.

Insufflation of Oxygen Gas under Pressure in the Treatment of Empyema and Sinusitis of the Maxillary Antrum.—ORESCO (*Ann. des maladies de l'oreille, du larynx, du nez, et du pharynx*, November, 1906) reports eleven successive cases successfully treated by intranasal puncture, washing with bichloride or phenol solution, and followed by insufflations of compressed oxygen gas under two hundred and fifty pounds' pressure.

Clinical Forms of Cancer of the Maxillary Sinus.—SEBILEAU (*Ann. des maladies de l'oreille, du larynx, du nez, et du pharynx*, November, 1906), based upon some thirty cases observed by him in the course of four years, of which but two were surviving, divides the clinical forms into three: neoplastic, suppurative and infectious, and putrid or gangrenous. He shows that the suppurative form is often mistaken for maxillary sinusitis or for panusitis, and that the mistaken diagnosis is sometimes inevitable.

The Tonsil as a Focus for Tuberculosis.—CHAS. M. ROBERTSON (*Jour. Amer. Med. Assoc.*, November 24, 1906) gives an anatomical description of the tonsil and reports his researches, tracing direct infection from the tonsils through the cervical lymphatics to the lymphatics of the pleura and thence to the apex of the lung. In studying 232 patients whom he had operated upon, he found that 8 per cent. presented undoubted tuberculous lesions in the form of giant cells and tuberculous-tissue change, the greater number of tonsils having been of the so-called submerged type. He therefore advocates the complete extraction of the diseased tonsils. This he does either under cocaine anesthesia or ethyl chloride preferably, with specially devised scissors, of which illustrations and descriptions are given.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Cause of the Increased Portal Pressure in Portal Cirrhosis.—HERRICK (*Jour. Exp. Med.*, 1907, ix, 93) has investigated this problem by injecting washed livers, and has observed the pressure influences of the hepatic and the portal circulations upon one another in normal and cirrhotic livers. The arterial and portal injections were varied together as to their pressures, then the arterial circulation alone, and finally the portal circulation alone, were studied in order to ascertain their behavior under various pressure conditions. It was found that the portal circulation was as free in cirrhotic livers as in normal livers, thus casting doubt upon the generally accepted ideas of the cause of ascites in cirrhosis. Herrick found that when the pressure in the hepatic artery was raised from 0 to 130 mm. Hg. the pressure in the portal vein in normal livers rose but 3 or 4 mm. Hg., while in cirrhotic livers this rise of pressure in the hepatic artery produced a rise in the portal vein of 20 or 30 mm. Hg. This is due to the fact that in cirrhotic livers there is a far greater communication between the arterial and portal currents than in normal livers.

Herrick believes that the factors contributing to the increased portal pressure in portal cirrhosis are: (1) The direct communication of the arterial pressure to the portal vessels through dilated capillaries, and (2) the larger volume flow of the hepatic artery in proportion to the portal flow in cirrhosis as compared to that in the normal liver. When salt solution was injected into the hepatic artery it was found to return by the portal as well as by the hepatic vein, while from a portal inflow the return was through the hepatic vein only. The portal pressure has a decided influence on the volume flow in the hepatic artery, and *vice versa*. This influence was found to be more marked in cirrhotic than in normal livers. The communication of the arterial pressure to the portal pressure is an important factor in explaining the increased portal pressure in portal cirrhosis.

The Pathology of the Liver in Cardiac Disease, and its Clinical Lessons.—SALAMAN (*Lancet*, 1907, i, 4) discusses the changes that take place in the liver when it has been subjected to stasis of blood and back flow. He advances the idea that the liver acts physiologically as a safety-valve to the heart, and that this action is definitely altered by the changes produced by congestion. He finds that a normal adult liver will take up fluid equal in volume to that of the liver itself, if the portal vein has been tied and the injection is made through the hepatic vein, at a pressure of two feet and three inches of water, the pressure of the right

ventricle. When a pressure of one foot of water, that equal to the pressure of the right auricle, is maintained, the liver takes up fluid equal in volume to about one-half or three-fourths of its own volume. When the pressure is released the liver recoils by its own elasticity and about two-thirds of the injected fluid is expelled. Salaman believes that with the aid of the intra-abdominal pressure it is possible for all of the absorbed fluid to be expelled.

This experiment was then tried on three types of livers which had been subjected to engorgement for longer or shorter periods. With only recent engorgement and with fatty but no fibrous changes, it was found that the capacity of the liver for taking up injected fluid was not impaired, while the recoil was much less than normal. In livers moderately fibrosed, congested and nutmeg in type, the capacity for absorbing fluid was found distinctly reduced, while there was an increase in the recoil of the liver when the pressure was removed. When the cirrhotic nutmeg liver, with portal, hepatic, and central fibrosis, was used it was found that its capacity for absorption was still more reduced, and that the recoil was not so great as in the second type.

From these facts Salaman concludes that under conditions of cardiac stress the liver will draw off a large volume of blood from the right auricle, and that after a time this property of distensibility is distinctly impaired by fibrous changes, which changes, however, increase the force of the liver's recoil and prevent its use as a reservoir for blood. In complete cardiac compensation there is no engorgement of the heart and no back pressure. While the liver may be looked upon as a sponge-like safety-valve to the heart, continued use of this safety-valve action leads to its own abolition. Salaman believes that liver pain, œdema, and ascites in heart disease may be symptoms of broken compensation in the liver.

The Leukolytic Action of the Blood Serum of Cases of Leukemia Treated with X-rays, and the Injection of Human Leukolytic Serum in a Case of Leukemia.—Capps and Smith (*Jour. Exp. Med.*, 1907, ix, 51) have carried on a series of experiments to determine the effect of the *x*-rays upon the leukocytes and the serum in cases of leukemia. They first injected normal human serum into rabbits and guinea-pigs, and found that this caused a rise of leukocytes in twenty-four hours of from 5 to 15 per cent. A second series of experiments showed that when the serum of cases of lymphatic leukemia untreated by *x*-rays was injected into rabbits and guinea-pigs, a greater increase in the leukocytes occurred than with normal serum, their increase being from 5 to 56 per cent. When serum from cases of leukemia treated with *x*-rays was used, however, a marked decrease in the number of leukocytes in the blood of rabbits and guinea-pigs was found. In a case of the lymphatic type, in which improvement in the clinical picture of the disease was greatest, the reduction was from 35 per cent. to 60 per cent., while in a case less improved the reduction was only from 10 to 20 per cent. In a much improved case of splenomyelogenous leukemia the leukocytes were reduced 12 per cent. and again 40 per cent.

Capps and Smith conclude that the amount of leukolytic substance present probably varies with the amount of improvement observed clinically in the cases. They exposed defibrinated human blood,

both from healthy individuals and from cases of leukemia *in vitro* to the *x*-rays and found practically no diminution in phagocytic power of the leukocytes. They think it improbable, therefore, that Quadrone is right in saying that several exposures of animals to the *x*-rays increase their resistance to infection by stimulating phagocytosis.

The effect of leukemic serum on human leukocytes and erythrocytes was studied by mixing these cells with the serum in hanging drops. It was found that leukemic serum which had not been exposed to the *x*-rays had no leukolytic action, nor were the erythrocytes changed by it. The serum from *x*-rayed leukemic cases, however, was found to have a marked leukolytic action on leukocytes from normal individuals and from cases of leukemia. In the latter case the action seemed selective, and showed a marked preference for mononuclear cells and myelocytes. This serum agglutinated the red blood cells in the hanging-drop preparations. The *x*-rays were found to destroy leukocytes and produce a leukolytic substance in leukemic blood *in vitro*, but no such reaction was obtained with normal blood. The number of leukocytes in the circulating blood of leukemic cases was found to decrease after exposure to the *x*-rays. In order to test the action of the leukolytic serum on an untreated case of lymphatic leukemia the serum from a treated case which was known to be highly leukolytic was injected into the abdominal wall of an untreated case. Three injections were made, and each time there was a distinct reduction in the number of leukocytes by destruction principally of the mononuclear elements, but the reduction was always followed in a few days by a rise to or above the number before the injection. Capps and Smith think this leukolytic substance is probably formed by the destruction of the leukocytes.

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